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VIRTUAL LAF CONFERENCE

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SUBJECT: P Cells & Free Radicals

PC has proposed an exciting new topic for the Conference Room. I have always had a strong feeling that free radicals are somehow involved in AF and PC's studies certainly confirm this. Please join in the discussion to shed further light on this potentially preventable cause of AF.

Hans

P Cells and Free Radicals

P is for pole cells and they are the pacemaker cells of the heart. These have traditionally been described only in nodal tissue (SA node and AV node). However, in August of 2003 they were first described in human pulmonary veins (enter left atrium). Other subsequent reports have confirmed this. To date they have not been found in the vena cavae that enter the right atrium or anywhere else in the heart for that matter.

There have been numerous reports in the literature about the increasing success of catheter ablation via pulmonary vein isolation (PVI) (see Hans most recent AFIB report for an excellent discussion of this). Initially I thought that its success was due to transection of vagal nerve fibers that enter the left atrium via its pulmonary veins. The increase in HR post ablation certainly testifies to this event. However, vagal nerve fibers to the SA node travel along the superior vena cava (right atrium) and yet this doesn't seem to be a player in the PVI success story. Accordingly, I have become more interested and would like to share my research into the matter and hear your thoughts here in the CR.

Pacemaker cells are unique in that they slowly depolarize by themselves, hence their greater inherent automaticity. This is due to their unique Na and K ion channels.

Acetylcholine (ACh) released from the vagus nerve endings binds to muscarinic receptors on the pacemaker cells. ACh not only affects K channels but also a unique Na channel (AKA the funny current). In fact cardiac pacemaker activity is regulated by at least five different classes of ion channels and by the opposing influence of sympathetic and parasympathetic stimulation.

In September of 1998 the Bordeaux group published an EP study of 45 patients with frequent paroxysmal AF. They looked at the location of the triggering atrial ectopic beats and found that 94% were located in the PVs (2-4 cm inside the veins). I'm not sure what per cent of those with paroxysmal AF qualify as lone (LAF), but I would guess that if one accepts any degree of hypertension in the definition of LAF, it would be a majority.

In October of 2002 this same group published an EP study of 28 patients with paroxysmal AF (average age about 50) v. 20 age matched controls. They evaluated the effective refractory period (ERP) of cells in the pulmonary veins and the left atrium in both groups. They found that left atrial ERP did not differ between the two groups. However, in the AF group the PV ERPs (v. the LA ERPs) were shorter whereas in the control group they were longer. Furthermore, they

found that there was greater dispersion of PV conduction velocity in the AF patients and that in these same patients AF was more easily induced (by fast pacing) in the PVs (22/90) than in the left atrium (1/81). Incidentally dispersion of conduction velocity is now believed to be more instrumental in the initiation of AF than dispersion of refractoriness. Consequently, these PV refractoriness and conduction properties create a substrate favorable for reentry. It would appear to me that these PVs represent the oft quoted but elusive "defective substrate" of LAF. This is what is responsible for "the loss of physiologic rate adaptation" present in AF, i.e., conditions that should slow down the heart (slower conduction velocity, shortened refractory period) often result in a tachyarrhythmia instead.

Putting these two studies together paroxysmal AFers appear to have a problem with their PVs. It would seem logical to implicate P cells in this process. In December of 2003 there was a nice review article in the Journal of Cardiovascular Electrophysiology entitled "Basic Electrophysiology of the Pulmonary Veins and Their Role in Atrial Fibrillation: Precipitators, Perpetuators, and Perplexers", summarizing that state of affairs to date on paroxysmal AF. You can read it at

http://www.blackwell-synergy.com/links/doi/10.1046/j.1540-8167.2003.03445.x/full/?func=showHome#h1

but you might have to register first (it's free).

Recently it was mentioned in an article posted on the BB that the PVs not only initiate AF but also contribute to its maintenance. I can't remember who posted the article but Erling picked up on the tidbit. It appears that this venous tachycardia (AKA "PV bursting") emerges during AF but not in AF induced in normal hearts. This was a canine study. A majority of those with paroxysmal AF have this PV tachycardia during AF and it is much more often intermittent than continuous. In a recent sheep study this bursting was enhanced by increasing intraatrial pressure. This leads to the question of whether transition to chronic AF is more a function of atrial enlargement per se (ability to accommodate more wavelets) or to the increased intraatrial pressure caused by prolonged intermittent AF that causes that enlargement.

The changes in the ERP that are present in those with paroxysmal AF appear to be due to many ion channels (inward L-type Ca channels, several K channels and sodium channels). Initially many (inc me) have felt that a specific ion channelopathy was the culprit for LAF. A K channel polymorphism (a mutation present in more than 1% of the general population) seemed likely. However, given recent information, it would appear that it is not nearly that simple (what a surprise!). This simplistic view has also been responsible for my failure to completely embrace the inflammation/oxidative stress hypothesis in the genesis of LAF. I previously had thought that damage due to inflammation was far too broad to manifest only as a simple channelopathy without other evidence of heart disease (LAF).

Once convinced that oxidative damage is at the center of LAF one must decide how and why this happens to the P cells in the PVs v the SA and/or AV nodes. I think the answer lies in the relationship between the lungs and the left atrium. The former are a constant source of free radicals from cigarette smoke, allergens, ozone and just air pollution in general. These have been implicated in a long list of pulmonary diseases. Hans on pp. 137-138 in his book LAF: Towards a Cure has suggested that "high oxygen pressure and shear stress (present in the pulmonary veins) is a potent breeding ground for reactive oxygen species (ROS)". He further suggests that exercise might contribute to this. Whether the high association of LAF in endurance athletes is due to excess vagal tone or actual P cell damage has not yet been determined.

Free radicals attack cell membranes as well as nuclear and mitochondrial DNA. This general process is called oxidative stress. Membrane damage due to free radicals is called lipid peroxidation and this is felt to be the mechanism responsible for the well known development of AF after coronary artery bypass grafting (CABG) via ischemia/reperfusion damage. This is just a fancy way to describe what Hans is saying. Ion channel damage would loom large in the lipid peroxidation scenario.

Sometime last year I believe Richard posted on the BB an article written in December 2003 entitled
Atrial Fibrillation: Are We Treating the Right Disease?

http://www.medscape.com/viewarticle/463648_print

That article presents lots of data linking redox state with arrhythmia. Redox is short for reduction/oxidation, which refers to the gain or loss respectively of electrons caused by free radicals. David van Wagoner of the Cleveland Clinic in an article written sometime after May 2002 addressed the issue of oxidative stress and AF. This can be viewed at

http://www.clevelandclinic.org/heartcenter/pub/atrial_fibrillation/AFresearch.htm#oxidativestress_studies

He points out that AF is associated with calcium overload, which can increase the production of free radicals. If you buy the oxidative stress hypothesis, then this explains the "AF begets AF" observation. Numerous studies have documented an inverse relationship between the levels of free radicals and their scavengers such as vitamins A, C, and E, magnesium and selenium. There are numerous studies touting the preventative effects of preoperative Mg and Vitamin C on the development of AF post CABG.

Furthermore, one can measure the cellular damage caused by oxidative stress through its biochemical markers. High sensitivity C reactive protein (hs CRP) would be at the top of this list. For years mainstream medicine has "shouted from the mountaintops" the dangers of cholesterol. The NIH spent millions of dollars trying (and failing) to show a relationship between dietary cholesterol and heart disease. High blood cholesterol, which is associated with heart disease, is largely genetically determined. But it is less important than an elevated CRP in predicting future heart disease. Although this is not exactly late breaking news, please visit

http://www.usatoday.com/news/health/2005-01-05-heart-inflame_x.htm

to read an article on this that appeared in a major newspaper today.

Having said all this, why doesn't everyone have AF? There are many cardiac ion channels. In fact there are several hundred K channels alone. IMHO there must be hundreds of polymorphisms yet to be discovered that involve P cell ion channels. If the mix of polymorphisms is right (or more appropriately, wrong) and sufficient cell membrane (and ion channel) damage due to free radicals has occurred, then AF will appear in these genetically predisposed individuals. IMHO don't hold your breath waiting for the announcement about some single genetic ion channelopathy that will explain the growing epidemic of LAF.

PC

Aloha

I forgot to add something that I'm sure Jackie and all you astute nutritionists will point out.

Dr. Lam (www.lammd.com) estimates that each cell in the body undergoes 100,000 "hits" by free radicals everyday.

However, this mushrooming epidemic is due not only to the concomitant increase in environmental free radicals but also to the general decline in the quality of our food. We can no longer obtain the required antioxidants through diet alone. Mainstream medicine has again been slow to step up to the plate and recognize this fact. The pharmaceutical industry is in large part responsible for this. Better to take a pill for what ails you. But the general public is not blameless in this affair. Most patients don't want to be told to lose weight, stop smoking and eat their fruits and veggies. "Just gimme a pill doc." And if he doesn't they'll find one that will.

But we know better I hope (see Jackie's recent BB post on this).

PC

PC,

I hope you're enjoying your new home in Hawaii, as well as staying AF free. I haven't been reading everything of late,

as I've been so busy, but this post peaked my interest. Happy New Year to all, btw!!

I do believe that free radicals could be the attributing factor for the many epidemic diseases that are going on in our society. It just depends on what your genetic weakness is, as to what you will be plagued with.

In my case, my CRP and Homocysteine levels were normal, buy my lipid peroxidation levels were high, and on the same test, my glutathione levels were low. Along with Glutathione being low, all my sulfur containing aminos were also low. As mentioned in previous posts, sulfur, wants two electrons to complete it's outer shell, and it will attach to free radicals for removal from the body. In the case of glutathione, it will take the free radical from Vit. C, to carry it out of the body, and then leave Vit C to carry on attaching to another free radical. In other words it helps C recycle. The lungs have about 140x's more glutathione than other parts of the body, and this is why Valerie Hudson was having such remarkable results with administering nebulized (inhaled) glutathione to her 3 sons with the genetic disorder, Cystic Fibrosis. There was also a previous post of a 95 yr. old man in a wheelchair, and on oxygen, with COPD, that after 2 or 3 days on nebulized glutathione, was able to eliminate his oxygen and get out of his wheelchair.
That's amazing, to say the least.

Because the blood is leaving the lungs and entering the pul. veins to the left atrium, it would only make sense that if there wasn't enough glutathione to attach to the free radicals in the lungs, then these radicals would be left to cause destruction downstream. But then why would some have clockwork, intermittent episodes? My hypothesis on this, is that the brain is extremely intelligent, and as I've said in the past, it has to make decisions about where to send the sulfur. Because we are all low in sulfur, due to our environment, the brain HAS to make these decisions for methylation between neurotransmitters and fatty acids, as well as removal of free radicals. In Jackie's recent post, it was stated that if methylation isn't happening then one is presented w/GERD, as well. All of the aminos that are important for heart health always lead back to the sulfur containing aminos, carnitine and taurine, too.

So, in trying to write this with many interruptions (teenagers on a Friday night), I'm basically saying that the sulfur aminos are critical to our health in present day conditions, and for calming the bouncing electrons/free radicals, but we must NEVER forget about Mg, B6, C and K, as well, because those are in short supply, as well.

I hope this all made sense.

Richard

PC - Thanks for taking a hula break to post this. Good information and undoubtedly the reason why for the ablations...at least with Dr. Natale, he said he just goes for the PV area immediately since that's the place they found most of the potentials to be. He does also check all the other areas during ablation and often finds potentials in the area of the superior vena cava.

Additionally, while he doesn't do the statin protocol post ablation now, as he did with me a year ago, he explained that because of the oxidized LDL in the PV area, they liked to put patients on statins (Lipitor) for at least a month post-ablation to help reduce inflammation from in this area. Again, this relates to your findings and makes sense. Although, now he doesn't require the Lipitor, or so I hear. Perhaps they were doing a study on Lipitor at the time but found that they still had zero stenosis with or without since the ICE monitor virtually eliminates stenosis.

I have collected some data both from the convention and other resources that points exactly to what you mention about antioxidants and free radical damage. I'll review to see if anything significant is mentioned that will enhance your excellent post and observations.

And yes the food is part of the problem and true, people are the other...I believe that's why supplements with superior antioxidant properties were collectively emphasized. And, this would be more important in older people but not to be ignored by the younger, as well.

Repeating what Dr. Braverman said.... N acetyl cysteine is the ultimate, #1 antioxidant and everyone should be on it.

Jackie

In an effort to tackle ROS attack (and thinking of the Crayhon Protocol - recently re-brought to my attention by Erling over on the forum) how does the following protocol sound to you guys?

N acetyl cysteine (how much/day?),
glutathione (ditto?),
Vit A from good quality cod liver oil,
Vit C from plenty of fruit and veggies,
Mag taurate to get Mg and Taurine,
Selenium 200mcg/day
CoQ10 & Carnitine..... (not directly involved with tackling ROS attack)

I'd still like to get everything from food ideally though..... Soooo hard to know EXACTLY what to do for the best.

Thanks PC for the most interesting post,

Mike F.

After I posted the previous, I was thinking back on the conversation I had 3 months after PVI... Dr. Natale was explaining about the potentials being in the PV area and very frequently, inside the PV, themselves. They don't like to ablate inside the veins because of the stenosis risk (obviously) but he said that the circumferential burns right at the ostia were working well....

He then went on to say that I had a common ostia for either two or three of the veins which made his ablation that much more difficult.... but at that point in time, zero stenosis was reported for me.

Jackie

Mike,

Your protocol sounds reasonable with a couple of modifications.

1. Taking glutathione orally is a waste of time and money as it does not increase blood levels of glutathione (1).

2. The best way of increasing glutathione levels is by supplementing with vitamin C. 500 mg three times a day should do the trick (1).

3. You did not mention vitamin E. Despite the recent, totally unwarranted, criticism of vitamin E, I still believe that taking 400 IU of a 50:50 mixture of gamma and alpha-tocopherol should be an essential part of any antioxidant program. If your supplement contains toco-trienols as well, so much the better.

4. You also did not mention alpha-lipoic acid. This antioxidant is very important as it helps to regenerate all the other antioxidants besides being a powerful antioxidant in its own right in both the lipid and water phase of the cells. 200-300 mg/day in divided doses is probably a reasonable amount.

You can find out a lot more about antioxidants by reading some of the research reports at my website:

http://www.afibbers.org/vitamins.htm

Please note that each article has a link to the IHN database where you can find the very latest information about the antioxidants.

Hans

(1)Murray, Michael T ND, Encyclopedia of nutritional Supplements, pp. 62-64. Prima Publishing 1996.

I've found some files on Oxidative Stress that may be of interest....

Chronic Diseases
Flavonoids - Disease Prevention
Oxidative Stress

Date: June 30, 2003

Re: **Effects of Flavonoid Intake on Oxidative Stress-related Chronic Diseases**

Knekt P, Kumpulainen J, Jarvinen R, et al. Flavonoid intake and risk of chronic diseases. *American Journal of Clinical Nutrition. 2002;76:560-568*.

Free oxygen radicals may be involved in the development of atherosclerosis, cancer, diabetes, asthma, rheumatoid arthritis, and cataract. Flavonoids are products of plant metabolism and are effective antioxidants; thus, they protect tissues against free oxygen radicals. Different flavonoids have different chemical structures and may have different effects on health. This study evaluated the effects of flavonoid intake on chronic diseases associated with oxidative stress.

The Finnish Mobile Clinic Health Examination Survey collected questionnaires from 65,440 people from 1966 to 1972. A thorough dietary history of each participant was collected. In 1997, intakes of flavonoids and nutrients were evaluated for all food items by collecting fruits, berries, vegetables, and beverages as well as performing chemical analyses. Incidence of cerebrovascular disease, cancer, asthma, type 2 diabetes, cataract, and rheumatoid arthritis were assessed 28-30 years later.

People with a higher flavonoid intake tended to have a lower total mortality. The association was mainly due to quercetin intake, especially from apples, onions, and oranges.

Ischemic heart disease tended to be lower at higher quercetin and kaempferol intakes.

Apple and onion intakes were significantly associated with a decrease in ischemic heart disease mortality.

The incidence of cerebrovascular disease leading to hospitalization or death was lower at higher intakes of kaempferol, hesperetin, and naringenin.

Orange, white cabbage, and grapefruit intakes showed the strongest associations with cerebrovascular occurrence.

Apple intake showed a significant association for thrombotic stroke.

The total cancer incidence was significantly lower at higher quercetin intakes, especially for lung cancer risk in men.

Prostate cancer risk was lower at higher myricetin intakes, and breast cancer risk tended to be lower at higher quercetin intakes. There was no association between flavonoid intake and occurrence of cancers of the stomach, colorectum, or urinary organs.

Apple intake was strongly associated with a lower risk of lung cancer. A higher intake of kaempferol was related to a high risk of rheumatoid arthritis.

Intake of white cabbage was strongly associated with an increase in rheumatoid factor-positive disease.

A lower risk of type 2 diabetes was associated with higher quercetin and myricetin intakes. Apple and berry intakes showed the strongest association.

Cataract incidence was not significantly lower at higher total flavonoid intake. The incidence of asthma was lower at higher total flavonoid intakes, especially quercetin, hesperetin, and naringenin. The strongest associations were noted for apple and orange intakes.

Increased apple intake was associated with a decreased occurrence of all cancers combined, lung cancer, asthma, type 2 diabetes, thrombotic stroke, total mortality, and ischemic heart disease mortality. The only disease with a suggestively elevated risk at higher apple intakes was rheumatoid arthritis.

It is not surprising that most beneficial effects were ascribed to quercetin, since it is considered the most potent antioxidant. Flavonols and flavonones protect against several chronic diseases. Alternately, foodstuffs rich in flavonoids may contain other unknown biologically active compounds.

For example, apples are a poor source of the antioxidants vitamin C and beta-carotene. Data on tea and red wine consumption were not available in the present study. However, consumption of tea, coffee, and red wine by the Finn population at the time of the study was low. One weakness of the study is that flavonoid intake may not be an accurate measure of flavonoids available in the body.

The results of this study are very interesting, and seem to support the saying that "an apple a day keeps the doctor away."

-Heather S. Oliff, Ph.D.
http://www.physiologics.com/herbclip/review.asp?i=43506

Summary article based on this study:

American Journal of Clinical Nutrition, Vol. 76, No. 3, 560-568, September 2002

Original Research Communication
Flavonoid intake and risk of chronic diseases1,2
Paul Knekt, Jorma Kumpulainen, Ritva Järvinen, Harri Rissanen, Markku Heliövaara, Antti Reunanen, Timo Hakulinen and Arpo Aromaa

From *Diabetes*

The Metabolic Syndrome, Circulating Oxidized LDL, and Risk of Myocardial Infarction in Well-Functioning Elderly People in the Health, Aging, and Body Composition

CohortPosted 04/28/2004 Paul Holvoet; Stephen B. Kritchevsky; Russell P. Tracy; Ann Mertens; Susan M. Rubin; Javed Butler; Bret Goodpaster; Tamara B. Harris

Abstract and Introduction

The object of this study was to establish the association between the metabolic syndrome and oxidized LDL (oxLDL) and to determine the risk for coronary heart disease (CHD) in relation to the metabolic syndrome and levels of oxLDL.

OxLDL was measured in plasma from 3,033 elderly participants in the Health, Aging, and Body Composition study. The metabolic syndrome was defined according to criteria established in the Third Report of the National Cholesterol Education Program Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults.

We observed that the metabolic syndrome was associated with higher levels of oxLDL due to a higher fraction of

oxLDL, not to higher levels of LDL cholesterol. Individuals with the metabolic syndrome had twice the odds of having high oxLDL (>1.90 mg/dl) compared with those not having the metabolic syndrome, after adjusting for age, sex, ethnicity, smoking status, and LDL cholesterol.

Among those participants who had the metabolic syndrome at study entry, incidence rates of future CHD events were 1.6-fold higher, after adjusting for age, sex, ethnicity, and smoking status. OxLDL was not an independent predictor of total CHD risk. However, those with high oxLDL showed a greater disposition to myocardial infarction (relative risk 2.25, 95% confidence interval 1.22-4.15). We concluded that the metabolic syndrome, a risk factor for CHD, is associated with higher levels of circulating oxLDL that are associated with a greater disposition to atherothrombotic coronary disease.IntroductionOxidized LDL (oxLDL) has been shown to play an important role in the pathogenesis of atherosclerosis.[1-3]

We and others have demonstrated an association between cardiovascular disease (CVD) and oxidation of LDL.[4-6] We have also found circulating oxLDL to be a prognostic marker of CVD in cardiac transplant patients.[7] In middle-aged people, obesity and dyslipidemia are the strongest predictors of levels of oxLDL.[8] Recently, the association between dyslipidemia and oxidation of LDL has been demonstrated in individuals in the pre-diabetic state.[9]

Finally, we have shown that in the Health, Aging, and Body Composition (Health ABC) cohort a high coronary heart disease (CHD) risk status (based on Framingham score) before CHD events is associated with high levels of circulating oxLDL, even after adjustment for LDL cholesterol.

[10]Individuals with the metabolic syndrome are at increased risk for developing CHD as well as for mortality from CHD and other causes.[11,12] The Third Report of the National Cholesterol Education Program Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (ATP III)[13] drew attention to the importance of the metabolic syndrome and provided a working definition of this syndrome.

Findings from the Third National Health and Nutrition Examination Survey (NHANES III) showed that the metabolic syndrome is highly prevalent within the U.S.; that prevalence increased from 6.7% among participants ages 20-29 years to 43.5 and 42.0% for participants ages 60-69 years and >/=70 years, respectively.[14]

Because the metabolic syndrome is associated with high risk for atherosclerotic disease, a process thought to involve LDL oxidation, we examined the relation between metabolic syndrome components and circulating oxLDL levels in the Health ABC cohort.

Because we have found an association between the metabolic syndrome and higher prevalence of high levels of oxLDL, we sought to evaluate in a large-scale elderly population the potential relation among the metabolic syndrome, circulating oxLDL, and incident CHD events.

http://www.medscape.com/viewarticle/473529?src=mp

Staying on Top of Oxidative Stress – Weston Price Foundation

By Stephen Byrnes, ND, RNCP

Oxidative stress (OS) is fast becoming the nutritional and medical buzzword for the 21st century. Implicated in a growing list of diseases, from cataracts to cancer, health-conscious people should take steps to protect themselves against the ravages of free radicals, the active criminals in OS.

Despite the growing dangers of OS, there are some simple, but powerful, weapons against it. An avoidance of factors that contribute to OS; a diet of whole, organic, unprocessed foods; and supplemental anti-oxidants, afford the best protection against this serious and insidious condition.Oxidative Stress (OS) is not, in and of itself, a disease but a condition that can lead to or accelerate it. OS occurs when the available supply of the body's antioxidants is insufficient to handle and neutralize free radicals of different types.

The result is massive cell damage that can result in cellular mutations, tissue breakdown and immune compromise. What are free radicals? They are highly unstable molecules that interact quickly and aggressively with other molecules in our bodies to create abnormal cells. They are capable of penetrating into the DNA of a cell and damaging its "blueprint" so that the cell will produce mutated cells that can then replicate without normal controls.

Free radicals are unstable because they have unpaired electrons in their molecular structure. This causes them to react almost instantly with any substance in their vicinity. Oxygen, or oxyl, free radicals are especially dangerous.

Surprisingly, however, free radicals are involved in many cellular functions and are a normal part of living. When, for example, a mitochondria within a cell burns glucose for fuel, the mitochondria oxidizes the glucose and in so doing generates free radicals. White blood cells also use free radicals to attack and destroy bacteria, viruses and virus-infected cells.

The detoxifying actions of the liver also require free radicals. Although free radicals have useful functions in the body under controlled conditions, they are extremely unstable molecules that can damage cells if left uncontrolled. Free radicals destroy cellular membranes; enzymes and DNA.

They accelerate aging and contribute to the development of many diseases, including cancer and heart disease. Its important to note here that free radicals are also released in the body from the breaking down or detoxification of various chemical compounds. Additionally, certain foods contain free radicals which, when eaten, enter the body and damage it.

The major sources of dietary free radicals are chemically-altered fats from commercial vegetable oils, vegetable shortening and all oils heated to very high temperatures.

ANTIOXIDANTS TO THE RESCUE

Fortunately, the body maintains a sophisticated system of chemical and biochemical defenses to control and neutralize free radicals. Chemical antioxidants scavenge free radicals, that is, they stabilize the unstable free radicals by giving them the electron they need to "calm down." The antioxidants are usually consumed or used up in this process—they sacrifice themselves.

The main antioxidants are vitamins A, E and C, betacarotene, glutathione, bioflavonoids, selenium, zinc, CoQ10 (ubiquinone), and various phyto-chemicals from herbs and foods. Green tea, for example, is rich in polyphenols—powerful antioxidants that help fight cancer.Biochemical antioxidants not only scavenge free radicals, but also inhibit their formation inside the body. These include lipoic acid, and repair enzymes such as catalase, superoxide dismutase (SOD), glutathione peroxidase. Melatonin, a hormone produced by the pineal gland, is also a potent antioxidant.

Cholesterol, produced by the liver, is another major antioxidant, which the body uses to repair damaged blood vessels. It is probably for this reason that serum cholesterol levels rise as people age. With age comes more free radical activity and in response the body produces more cholesterol to help contain and control the damage.Of all the antioxidants, glutathione appears to be pivotal. Made up of three amino acids (cysteine, glycine, and glutamic acid), glutathione is part of the antioxidant enzyme glutathione peroxidase and is THE major liver antioxidant.

It is a basic tenet of natural medicine that health cannot exist if the liver is toxic. Not surprisingly, extremely low levels of glutathione are found in people suffering from severe OS. People with AIDS, cancer and Parkinson's disease, for example, typically have very low glutathione levels.As noted earlier, oxidative stress occurs when the amount of free radicals in the body exceeds its pool of available antioxidants.

Obviously, knowing the varied sources of free radicals and avoiding them is an important part of minimizing their harmful effects.

WHERE DO THEY COME FROM?

As noted above, diet can be a major source of free radical stressors with processed or highly heated oils being the main offenders. If you are still using "foods" like refined vegetable oils, margarine or shortening (or "foods" made with them such as all commercial baked goods and "snack" chips), you need to remove them from your diet. Replace these

harmful fats with natural, cold pressed oils such as olive oil (which can be used for cooking) and small amounts of flax oil or walnut oil (which should never be heated).

Food grade, unrefined coconut oil and organic butter are also excellent choices, especially for cooking. Both of these naturally saturated fats are rich in certain fatty acids that have proven activity against bacteria, harmful yeasts, fungi and tumor cells. Additionally, since saturated fats (from animal foods and the tropical oils) and monounsaturated oils (from olive oil and cold-pressed nut oils) are more chemically stable, they are much less susceptible to oxidation and rancidity than their polyunsaturated cousins, which are mostly found in vegetable oils. As a general rule, then, although the body does require a small amount of naturally occurring polyunsaturated oils in the diet each day, it's best not to consume too much of them as they are more prone to free radical attack in the body. As Linus Pauling, PhD noted: "A diet high in unsaturated fatty acids, especially the polyunsaturated ones, can destroy the body's supply of vitamin E and cause muscular lesions, brain lesions, and degeneration of blood vessels.

Care must be taken not to include a large amount of polyunsaurated oil in the dietThe best food sources for polyunsaturates are fish, flax oil, sesame oil, walnut oil and dark green, leafy vegetables.

One caveat: canola oil is not recommended due to its chemical instability and its content of trans-fatty acids (TFAs), formed during processing. TFAs are increasingly being linked wtih cancer, immune system dysfunction and heart disease.

Excessive sugar intake can also contribute to free radical damage. White and brown sugars, and even sugar from so-called natural sources, such as fruit and fruit juices, maple syrup and honey, get converted into triglycerides by the liver and are subject to free radical damage. These damaged fats then promptly attack your arteries and directly contribute to cardiovascular disease.

Additionally, cancer and tumor cells feed off of sugar. It is for this reason that excessive sugar intake correlates very strongly with heart disease, cancer and a host of other ailments.

Poor nutrition in general contributes to OS. When the body is fed poorly, it slowly starves and all of its systems suffer. Weak organ systems are prime targets for free radical attack.

Free radicals are also released in the body from the detoxification of drugs (whether legal or illegal), artificial food colorings and flavorings, smog, preservatives in processed foods, alcohol, cigarette smoke, chlorinated drinking water, pesticides, radiation, cleaning fluids, heavy metals such as cadmium and lead, and assorted chemicals such as solvent traces found in processed foods and aromatic hydrocarbons such as benzene and naphthalene (found in moth balls).

Even psychological and emotional stress can contribute to OS. When the body is under stress, it produces certain hormones that generate free radicals. Moreover, the liver must eventually detoxify them and that process also generates free radicals.

Heightened OS has also been observed in athletes after intensive workouts due to the physical stress placed on the body. Both physical and emotional stress also prompt the release of endogenous cortisol, an adrenal hormone that reduces inflammation, but also suppresses the immune system. It should be obvious that all of us are exposed to free radicals from a variety of sources. Those of us living in cities are exposed to very high levels due to increased smog and pollution. Certainly, all of us need to take preventive action. If not, we could face the following conditions in our futures.

DETERMINING OS

When OS occurs, certain by-products are left behind that are excreted by the body, mostly in the urine. These by-products are oxidized DNA bases, lipid peroxides, and malonidialdehyde from damaged lipids and proteins.

The higher the levels of these various markers, the greater the chance there is of an OS-induced disease, or the aggravation and acceleration of an existing one. People with Down's Syndrome, for example, a genetic disorder, are subject to enormous OS due to increased cellular production of hydrogen peroxide, a potent oxidising agent, and frequently develop Alzheimer's-like conditions in their 30s.

These tests can be ordered by a doctor, naturopath or nutritionist. If you are concerned, ask your health care provider.

Even if you do not have access to formal testing, anyone can do the following simple test to see how much the body has been affected by free radicals: hold out your hand, palm down, in a relaxed position. Pinch the skin on the back of the hand, lift up the fold and then release it. If you have minimal free radical damage, the skin will snap back into place quickly. If the skin takes a few seconds to go back into place, this is not a good sign and action must be taken.

SOLUTIONS TO OS

Obviously, the first step is to avoid as much as possible the various stressors listed earlier. The next step is to adjust one's diet to include those foods and herbs rich in antioxidants. The last step is to consider supplementation.

Supplementation is recommended if one lives in a polluted environment, is subject to extreme stress, smokes, or has a condition associated with OS. Food sources of antioxidants are best. (See above.)

SUPPLEMENTS

Studies have shown that antioxidants work best in combination. Although there is value in supplementing with extra amounts of one or two antioxidants, better results are always obtained when a "cocktail" is administered. The reason for this is simple logic: different antioxidants neutralise different free radicals. If you take a combination, then more free radicals will be neutralised.

You can, however, "slant" the antioxidant effect towards a particular ailment or organ if the nutrient has a particular affinity to them. For example, glutathione would be recommended for hepatitis, Parkinson's, AIDS and liver disease; vitamins E and C would be recommended for arteriosclerosis; CoQ10 would be recommended for heart disease; and alpha lipoic acid would be recommended for diabetes.

See your health care professional to help you select the best antioxidant combination for you.Staying on top of oxidative stress is a necessity in our increasingly toxic world. Taking care to avoid those toxins as much as possible and to enrich our diets with life-giving antioxidants is a wise step to take in our endless quest for wellness.

RESOURCES·

For more technical papers on oxidative stress, see www.virusmyth.com ·For more info on coconut oil, see www.lauric.org

For more info on testing for OS: ICMT, 1305 Richmond Rd., Ottawa, Ontario K2B 7Y4, Canada; (613) 820-6755.

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About the Author
The late Stephen Byrnes was a nutritionist and naturopath. Visit his website at www.PowerHealth.net to read more of his articles.

Illnesses Associated With Oxidative Stress

GI Tract: Diabetes, pancreatitis, liver damage, and leaky gut syndrome
Brain and Nervous System: Parkinson's disease, Alzheimer's disease, hypertension and multiple sclerosis
Heart & Blood Vessels: Atherosclerosis, coronary thrombosis.Lungs: Asthma, emphysema, chronic pulmonary disease.
Eyes: Cataracts, retinopathy, macular degeneration.
Joints: Rheumatoid arthritis
Kidneys: Glomerulonephritis
Skin: "Age spots," vitiligo, wrinkles.
Body in General: Accelerated aging, cancer, autoimmune diseases, inflammatory states, AIDS and lupus.

Food sources of Antioxidants

CoQ10 (ubiquinone): Beef heart, beef liver, sardines, spinach, peanuts

Betacarotene: All orange and yellow fruits and vegetables; dark green vegetables

Zinc: Oysters, herring, lamb, whole grains

Selenium: Butter, meats, seafood, whole grains

Vitamin A: Cod liver oil, butter, liver, all oily fish

Vitamin E: Cold-pressed, unrefined nut and seed oils; wheat germ oil

Vitamin C: Berries, greens, broccoli, kale, kiwi, parsley, guava

Glutathione (GSH): Fresh fruits and vegetables, fresh meats, low-heat dried whey
Bioflavonoids: Most fruits and vegetables, buckwheat

Polyphenols: Green tea, berries.

Herbal Sources: Milk thistle, ginkgo biloba, tumeric, curry (Padma 28, a packaged Ayurvedic herbal formula, is a special blend of herbal antioxidants.)

NOTE: Try to purchase organic foods to minimize pesticide and hormonal residues. This article appeared in Wise Traditions in Food, Farming and the Healing Arts, the quarterly magazine of the Weston A. Price Foundation, Spring 2000This page was posted on 05/28/03

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CAUSES AND NUTRITIONAL THERAPIES FOR NEURODEGENERATIVE DISEASES

The Theron G. Randolph Lecture at the 35th Annual Meeting of the American Academy of Environmental Medicine (AAEM) was presented by David Perlmutter, MD, who titled his lecture

"Powerful Nutritional Therapies to Mitigate Neuroinflammatory Disorders."

The late Dr. Randolph was a founding member of the NOHA Professional Advisory Board. The following article just touches on Dr. Perlmutter's overall model for these diseases and on the therapies that he covered.

Neurodegenerative diseases, such as Alzheimer's, Parkinson's, and ALS (amyotrophic lateral sclerosis or Lou Gehrig's disease), have been shown to have many seemingly disparate causative factors, including foreign toxins from the environment (xenobiotics), infectious agents, genetic predispositions, toxins formed by our own metabolism1, electromagnetic radiation exposure, sex hormones, and pharmaceutical drugs. Interestingly, Dr. Perlmutter presents an overall understanding of these injuries, which specifically involves the mitochondria.

Agents triggering the cascade leading to the death of neurons in genetically susceptible individuals include toxins from the microorganisms in the gut, toxic metals and pesticides, food and environmental antigens, stress responses, and chronic infection.

Mitochondria are tiny structures within our cells and enclosed by their own membranes. They are the principal sites of ATP (adenosine triphosphate: our body's principal molecule for energy) production and they contain their own DNA (deoxyribonucleic acid) and ribosomes, replicate independently, and make some of their own proteins.

In addition to the neurodegenerative diseases, inadequate energy production by the mitochondria is involved in many other diseases, including even stroke like episodes. Often, the mitochrondrial DNA becomes abnormal. "Oxidative damage to mitochrondrial DNA has been estimated to be 10-fold higher than damage to nuclear DNA" (in other words, to the DNA for the division of our cells).

The cornerstone of this emerging model seems to focus on the critically important role of mitochrondrial energy metabolism and its relationship to the toxic effects of excitatory neurotransmitters. In this model excitatory neurotransmitters (predominantly glutamate2) stimulate specific neuronal receptors, which, when altered by deficient ATP production leads to a self-perpetuating cascade of events ultimately culminating in neuronal death. Mitochrondrial dysfunction has many deleterious consequences.

However, possibly the most important is a change in the electrical potential across the membranes of the neurons in our brains. With normal mitochrondrial ATP production the magnesium ion blocks a receptor for the excitatory neurotransmitter glutamate. However, with inadequate mitochrondrial energy production the control is gone and calcium floods into the cell. The influx of calcium is pivotal in the cascade of events that leads to the death of the neuron.2

Mitochondria are tiny structures within our cells and enclosed by their own membranes. . . . Inadequate energy production by the mitochondria is involved in many other diseases, including even stroke like episodes.

"It is interesting to note that in Parkinson's disease, Huntingon's chorea, and Alzheimer's disease, mitochrondrial dysfunction leading to excessive free-radical production and oxidative tissue damage seems to be confined to the brain, despite the fact that the underlying mitochrondrial abnormality is systemic. . . .

This may be explained by the unique susceptibility of the brain to mitochrondrial dysfunction and resultant excessive free-radical production since the brain uses approximately twenty percent of the total O2 consumption (while representing only one-fiftieth of the body weight)."

"It has long been known that there is a significant relationship between previous xenobiotic exposure and the risk of various neurodegenerative diseases, including Alzheimer's disease, Parkinson's disease, and amyotrophic lateral sclerosis. . . .

If indeed [as described above] mitochrondrial dysfunction plays an important role in the pathogenesis of neurodegenerative diseases and the various studies indicating increased risk with xenobiotic exposure are valid, what mechanism could relate these two concepts?"

Replying, Dr. Permutter points out: Research has shown that certain xenobiotics inhibit energy production in our mitochondria.

The question remains: Why are some people able to detoxify all the toxins and others cannot. Dr. Sidney Baker presented NOHA with fascinating material on "Detoxification and Healing,"1 including material on the sulfur-containing amino acids, especially methionine, and the production of glutathione with its powerful detoxifying potential.

Since the glutamate cascade is crucial in the destruction of neurons, a first step needs to be to avoid the ingestion of free glutamic acid (MSG), which is overwhelmingly prevalent in processed foods.

Dr. Perlmutter presented the AAEM conference with many possibilities for increasing our detoxifying potential. Quite a few have already been covered extensively in NOHA lectures and newsletters.

Since the glutamate cascade is crucial in the destruction of neurons, a first step needs to be to avoid the ingestion of free glutamic acid (MSG), which is overwhelmingly prevalent in processed foods.

2 (See, for example, NOHA NEWS, Spring 2000, "Free Glutamic Acid (MSG): Sources and Dangers.")

Dr. Perlmutter points out that antioxidants are essential in combating the oxidative stress to the neurons. As well as vitamins C and E, he mentions Coenzyme Q-10 as "one of the most promising agents for up-regulation of mitochrondrial function."

"Phosphatidylserine [a form of lecithin, a phospholipid, which contains the amino acid serine3] enhances both neuronal and mitochrondrial stability and activity and reduces mitochrondrial free-radical production." A study at Stanford University School of Medicine showed learning and memory improvement in the majority of treated patients compared to controls. (See Lecithin lecture.

3)Dr. Perlmutter mentions acetyl-L-carnitine for increased cellular ATP production. (See The Carnitine Miracle4) "Apha-lipoic acid5 is emerging as one of the most promising agents for neuro-protection in neurodegenerative diseases. This potent antioxidant demonstrates excellent blood-brain barrier penetration. It acts as a metal chelator for ferrous iron, copper, and cadmium, and also participates in the regeneration of endogenous antioxidants including vitamins C and E, and glutathione."

"The lipophilic [fat-loving] antioxidant vitamin E is thought to play a major role in defending mitochondria against oxidative stress." Our October 2000 NOHA lecturer gave a fascinating presentation on "The Vitamin E Factor: The miraculous antioxidant for the prevention and treatment of heart disease, cancer, and aging. WHAT'S MISSING FROM YOUR VITAMIN E CAPSULE"6

The hormone melatonin has properties that could make it useful in neurodegenerative conditions. It is a free radical scavenger and increases the gene expression for powerful antioxidant enzymes. Melatonin is both lipid and aqueous soluble and easily passes the blood-brain barrier.7

Dr. Bland notes that this cascade with the uncoupling of mitochondrial energy production in the neurons and the release of unquenched oxidants "is observed not only in neurodegenerative diseases, but also with less severity in chronic fatigue syndrome, fibromyalgia, multiple chemical sensitivity, and in individuals with Gulf War Syndrome."

Dr. Perlmutter mentions a number of herbal medications that have been found to be helpful for neurodegenerative diseases. Some of them act by reducing the production of nitric oxide. As we know, the free radical nitric oxide with its unpaired electron is important for penile erection. (See NOHA NEWS, Fall 99, page 3, "Nitric Oxide.")

When many toxic exposures put our immune systems in overdrive, we produce more nitric oxide (formula: NO) and the highly reactive oxidant-superoxide. When these two react together, they are most effective at the final killing of neurons. One researcher titled his article, "The Brain on Fire?"

Among the herbs mentioned by Dr. Perlmutter are silymarin (milk thistle), and Ginkgo biloba. In his interesting introduction to Dr. Perlmutter's monograph for the AAEM meetings, NOHA Honorary Member Jeffrey Bland, PhD, praises Dr. Perlmutter highly and also gives a summary of the model presented by Dr. Perlmutter. Dr. Bland states that Dr. Perlmutter gives us "an integrated model of neurodegeneration coupling genetics, environment, nutrition, lifestyle, and infection."

Agents triggering the cascade leading to the death of neurons in genetically susceptible individuals include toxins from the microorganisms in the gut, toxic metals and pesticides, food and environmental antigens, stress responses, and

chronic infection.

Dr. Bland notes that this cascade with the uncoupling of mitochondrial energy production in the neurons and the release of unquenched oxidants "is observed not only in neurodegenerative diseases, but also with less severity in chronic fatigue syndrome, fibromyalgia, multiple chemical sensitivity, and in individuals with Gulf War Syndrome."

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1See NOHA tape #165, "Detoxification and Healing-Key to Optimal Health" by Sidney M. Baker, MD, March 1998; and NOHA NEWS, "Detoxification and Healing," XXIII(4):1-3, Fall 1998.
2We have tapes and articles on the excitotoxins MSG and Aspartame. (The latter excitotoxin stimulates the exact same neuron receptors that are stimulated by glutamate. See Russell L. Blaylock, MD, Excitotoxins: The Taste that Kills: How Monosodium Glutamate, Aspartame (NutraSweet®) and Similar Substances Can Cause Harm to the Brain and Nervous System and Their Relationship to Neurodegenerative Diseases such as Alzheimer's, Lou Gehrig's Disease (ALS), and Others, page 28):
· See NOHA tape #149, "Food Additives and Brain Damage (MSG and Aspartame) by Russell L. Blaylock, MD, November 1995;
·See NOHA tape #112, "In Bad Taste: The MSG Syndrome," by George R. Schwartz, MD, September 1991;
·See NOHA tape #120, "Aspartame (NutraSweet®): Is It Safe?" by H. J. Roberts, MD, October 1992; and NOHA NEWS:
· "The Doctor's Corner: Trick or Treat?" by Theodore E. TePas, MD, (A report on adverse reactions from aspartame: NutraSweet®), XV(4):2-3, Fall 1990 [link];
·"Leaving a Bad Taste" (Review of In Bad Taste: The MSG Syndrome by George R Swartz, MD), XVI(1):3-4, Winter 1991 [link];
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·"Free Glutamic Acid (MSG): Sources and Dangers" (Report on NOHA lecture by Jack Samuels plus a review of the article by Adrienne Samuels, PhD, on deceptions by The Glutamate Industry), XXV(2):1-4, Spring 2000
3See NOHA tape #178, "Lecithin and Health" by Frank Orthoefer, PhD, who described vividly the advantages to the brain from lecithins containing high amounts of the amino acid serine, April 12, 2000.
4See NOHA tape #173, April, 1999, "Nutrition Made Simple" by Robert Crayhon, MS, author of The Carnitine Miracle and NOHA NEWS, "Optimal Nutrition," XXIV(3):2-3, Summer 1999.
5See NOHA tape #175, "The Next Millennium Anti-Oxidant: The Alpha-Lipoic Acid Breakthrough," by Burton Berkson, MD, PhD, September 1999.
6See NOHA tape #182, "The Vitamin E Factor: The miraculous antioxidant for the prevention and treatment of heart disease, cancer, and aging," by Andreas Papas, PhD, November 2000.
7See NOHA tape #156, "The Melatonin Miracle," by William Regelson, MD, May, 1996.
Article from NOHA NEWS, Vol. XXVI, No. 1, Winter 2001, pages 6-8.

L-Arginine's Vital Heart Health Connection

By Richard N. Podell, M.D.

Renewed interest in the neurotransmitter nitric oxide has researchers looking at its precursor, L-arginine, for treating certain kinds of heart disease. Once thought to be only a dangerous environmental pollutant and a poison, we now know nitric oxide is made in the body and it plays numerous roles including brain activity regulation and circulation control.

Administering nitric oxide for vasodilation has been a common practice for a long time but has only recently been understood. In World War I, doctors noticed that workers in ammunition factories who were packing shells with nitroglycerin had very low blood pressures. The observation eventually led to the development of a nitroglycerin pill for the rapid relief of angina–that is, exercise-induced chest pain caused by oxygen deficiency in the heart. In 1987 nitric oxide was determined to be the relaxant factor released by endothelial cells, explaining how nitroglycerin tablets help angina sufferers.

The body creates nitric oxide from the amino acid L-arginine, leading some to suggest arginine may also help those with angina. That said, people must understand the complexities of nitric oxide so they don't cause harm by selfdosing with arginine. Whether to take arginine should be decided with a medical professional.

To test arginine's potential, Polish physicians conducted a double-blind study involving 22 people with stable angina. Each subject took an exercise stress test, which was discontinued when changes on the electrocardiogram (EKG) indicated metabolic heart muscle strain. For three days half the group received placebo while the others took 1 g L-arginine twice daily. Participants then repeated the test.

Patients in the placebo group increased their exercise time by about one minute on the second test compared to the first (555 vs. 501 seconds). The arginine patients increased their time by nearly three minutes (from 531 to 700 seconds). After the sec ond test, EKG abnormalities were significantly less in the arginine group, even though they exercised longer.

It appears that in the short term arginine improves the exercise capacity of patients a, with stable angina. How? Because nitric oxide, synthe- sized from L-arginine, helps arterial blood vessels relax, permitting improved blood flow to the heart.2

Defective nitric oxide metabolism may be one reason people with heart disease commonly have impaired blood-vessel relaxation.3

So should patients with angina ask for L-arginine? Not necessarily and not yet. The study showing benefit for angina patients needs to be duplicated and extended for longer treatment periods before we can confidently apply its results.

Appreciating the Oxidative Effect

Both inherent and supplemental nitric oxide have intricate actions in the body, which can sometimes complicate illness. For example, high natural or induced levels of nitric oxide potentially can cause damage by increasing free radical generation (oxidative stress)4 and by promoting inflammation.

Nitric oxide molecules might be among those that stimulate oxidative stress in a heart attack, so elevated levels may worsen the prognosis for this condition. As a result, patients with congestive heart failure might respond better when their nitric oxide levels are lowered rather than raised.5

Clearly arginine and nitric oxide are not inert in human biochemistry. For one thing, their metabolism is intimately connected to the body's oxidative-stress balance. For example, people who take nitroglycerin often develop tolerance to the drug, meaning it stops working for them. To explain this, one theory proposes that nitric oxide-induced oxidative stress causes damage by depleting antioxidant defenses.

Following this clue, Japanese researchers found that vitamins C and E can block nitroglycerin tolerance.6 If antioxidant vitamins block nitric oxide's damaging effects, as suggested by the Japanese study, then supplying these may improve heart attack outcomes. Indian and Polish studies support the benefits of antioxidant vitamins in heart attack patients' follow-up care.7,8 In the Polish study, physicians gave vitamins C and E to some heart attack victims while others received standard cardiac care. Two weeks later, vitamin recipients had less oxidative stress in their white blood cells and less intense signs of heart muscle damage as judged by EKGs.

The good news is that natural products such as L-arginine and antioxidant vitamins have some power in treating various forms of heart disease. And although the majority of research is being done overseas, these studies are routinely published by America's best cardiology journals.

Prudence is required, however, because these natural products act on the body in complex ways not yet fully understood. Therefore, using these nutrients, especially L-arginine, requires both nutritional knowledge and good medical advice.

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Dr. Podell can be heard every Sunday evening, on The Willner Window Show, from 8 to 10 pm, WOR Radio.

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http://www.willner.com/References/webref28.htm

Following is a report from Great Smokies Labs incorporating information that Jeffery Bland, PhD, has compiled on Oxidative Stress.

I had some of this from a seminar and pieced together more from the GSDL web page.

Jackie (note the mention of Taurine, once again)

OXIDATIVE STRESS

For the past 25 years, physicians and researchers alike have studied oxidative stress in the body. More recently, attention has been focused on the many disorders tied into free radical chemistry (such as diabetes) and its strong link to the aging process.

Oxidative stress at the cellular level results from many factors, including exposure to alcohol, medications, trauma, cold, toxins or radiation. Although the biochemical significance of oxidative stress has been proven in relation to a vast range of degenerative disorders, including cancer, diabetes, premature aging, Alzheimer's and many others, until recently it has been difficult to assess its impact upon individuals and then measure effectiveness of therapeutic intervention.

Great Smokies Diagnostic Laboratory has developed a sensitive assessment utilizing acetaminophen and salicylate

challenges to evaluate oxidative stress status, antioxidant reserve and the interrelationship with hepatic detoxification. This test allows clinicians to develop individual therapies for patients and monitor treatment progress.

Oxidants and Antioxidants

Dr. Jeffrey Bland has published a comprehensive review of oxidants and antioxidants in clinical medicine, portions of which have been excerpted in the following discussion. Bland's review discusses oxidative stress in much greater detail than can be done herein, and is strongly recommended for additional reading.1

In a seminal paper published in 1957, Harman noted that free radicals increase with increasing metabolic activity and are related to alterations in biological oxidation/ reduction reactions.2 He suggested that aging and the degenerative diseases associated with it may be attributed to the deleterious side-effects of free radicals on cellular constituents and that antioxidants may play a very important role in helping to protect against free radical oxidative damage.

During the early 1970s, Irwin Fridovich posited that one of the most important oxidants in the cellular systems could be superoxide, which is created as a consequence of the univalent reduction of molecular oxygen to a free radical-like species.3

The late Linus Pauling was the first to propose that oxygen could be converted to superoxide by a variety of chemicals and physical methods and could be important in physiology. The birth of the field of free radical biology can be attributed in part to Pauling's pioneering work in inorganic chemistry, which occurred in the 1920s.4

More recently, Sies described the physiological state associated with increased production of reactive oxygen species (ROS) as a state of "oxidative stress."5 In 1985, he defined oxidative stress as a disturbance in the pro-oxidant/ antioxidant balance in favor of the pro-oxidant state. In this situation the organism is under increased exposure to reactive oxygen species which participate in free radical-induced alterations of cellular components through exponential chain radical-carrying mechanisms.

Oxidative Stress

Protection against the pathology induced by these oxidant species is provided by a broad class of protective agents termed antioxidants, represented by both the small molecules such as tocopherol and ascorbate, and enzymes such as superoxide dismutase and glutathione peroxidase.

Oxidative stress at the cellular level results from many factors, including exposure to alcohol, medications, trauma, cold, toxins or radiation. Oxidative stress also can be a consequence of liver exposure to xenobiotic substances which induce oxidative reactions through upregulation of the cytochrome P-450 mixed function oxidase system. This process can deplete specific cellular antioxidants such as glutathione, vitamin C or vitamin E.

Free Radicals

Free radicals can be generated in a wide variety of normal physiological functions. In some cases they are protective in nature but they can be harmful if not processed rapidly. Free radicals and lipid peroxides have been found to be elevated in patients with rheumatoid arthritis and systemic lupus erythematosus, as well as patients with glomerular disorders.6,7 They play an important role in regulating hypertension through the degradation of prostacyclin and nitric oxide.8

Free radicals have been implicated in the etiology of diabetes and potentially in some of its long term complications through the destruction of pancreatic beta cells.9 Notably, patients with Type I diabetes and angiopathy were found to have substantially higher lipid peroxides than controls, leading to the suggestion that this might be involved in the development of atherosclerosis.

Reactive oxygen species have also been implicated in the development of tissue damage in ulcerative colitis, in breast cancer risk where lipid peroxides were found to be highest in women with mammographic dysplasia, and in a variety of liver diseases.10-12

All these processes have the potential to impact one another through the free radicals that they generate.

The free radical mechanisms of the human body might be viewed in analogy to an army that has the potential for great good, but must be kept well disciplined and well fed. When exhausted by repeated attacks and poorly fed, this army has the potential for vast damage.

Using GSDL's Oxidative Stress Panel
The Oxidative Stress panel can be ordered by itself or in conjunction with the Detoxification Profile for a more complete picture of the body's detoxification function. The Oxidative Stress panel includes measurement of blood glutathione, lipid peroxides, Glutathione peroxidase (GSH-Px), Superoxide dismutase (SOD) and two derivatives of salicylate: catechol and 2, 3-dihydroxybenzoate (2,3-DHB).

Glutathione

The measurement of whole blood Reduced Glutathione reflects the body's reserves of this critical molecule. Glutathione functions both as an antioxidant (in the form of glutathione peroxidase) and as a detoxifying agent for a vast array of xenobiotics. Glutathione, for example, plays a critical role in detoxifying an intermediate of acetaminophen metabolism and preventing acetaminophen toxicity. Glutathione, due to its cysteine content, is also a minor source of the organic sulfate used in detoxification reactions. Glutathione is measured in a fasting plasma sample following an overnight acetaminophen challenge. This allows for assessment of functional reserve after detoxifying capacity has been tested.

Glutathione Peroxidase (GSH-Px)
Glutathione peroxidase is a selenium-dependant enzyme found primarily in the cytoplasm (70%) but also in the mitochondria (30%). Requiring four selenium atoms per active molecule, GSH-Px scavenges lipid peroxides throughout the membrane surfaces and quenches H_2O_2, converting it to water. Accumulations of oxidized lipids in mitochondrial and cell membranes have deleterious effects on function. Adequate levels of GSH-Px prevent this accumulation. The enzyme also participates in regeneration of the reduced (active) form of vitamin C .

Studies indicate that low levels of GSH-Px activity are related to disease states.13-14 High levels of this enzyme have also been associated with certain conditions such as Alzheimer's dementia and Beta-Thalassemia minor.15-16 This perhaps reflects a response to increased amount of oxidative stress.

By measuring reduced glutathione, glutathione peroxidase, and the lipid peroxides, the clinician can evaluate the relationship involved in maintenance of oxidative stress protection. Perhaps most importantly, evidence exists that supplementation with selenium is able to increase the levels of glutathione peroxidase in patients.17

Superoxide Dismutase (SOD)

This important enzyme is found in both the cell cytosol and the mitochondria. The cytosol form is dependant upon zinc and copper co-factors while the mitochondrial form requires manganese. As the name denotes, the superoxide radical is the substrate upon which the enzyme works, converting it to the less reactive H_2O_2 four times faster than if the enzyme were not present.

As normal mitochondrial processes result in production of the superoxide radical, sufficient activity of Mn/SOD and GSH-Px protect this organelle from these damaging functional by-products. During periods of excessive muscular activity, this may be of particular importance. Investigations of SOD in clinical medicine include the observation that SOD is a sensitive marker for exposure to agricultural pesticides.18 SOD seems to be found at high levels in conditions such as systemic sclerosis, myositis, and malignant melanoma.19-21
SOD is decreased in patients with juvenile rheumatoid arthritis, affirming correlations of SOD and inflammation.22 SOD levels are also found to be low in patients with both early hyperglycemia AND impaired glucose tolerance.23 SOD levels were found to be low in experimental zinc deficiency research. This provides physicians with clear therapeutic rationale for modifying zinc nutriture.24

Lipid Peroxides and Hydroxyl Radical Markers

Lipid peroxides result from hydroxyl radical-attack on polyunsaturated fatty acids (PUFAs). Elevated levels of lipid peroxides are thus strongly suggestive of hydroxyl radical activity and reflect oxidative damage. The production of toxic radicals and metabolites is thought to be the main cause of much systemic damage. It has been suggested that hydroxyl radical attack upon membrane bound essential fatty acids (EFAs), leading to a loss of highly unsaturated EFAs, may have a direct relationship to EFA deficiencies, free radical damage and the aging process.25
Catechol and 2,3-DHB are direct products of hydroxyl radical attack upon salicylic acid.26,27 The amount of 2,3-DHB appearing in the urine after an aspirin challenge appears to be a direct reflection of hydroxyl radical concentrations.27

It is not surprising that 2,3-DHB has been reported to be a sensitive indicator of oxidative damage in diabetics.28 The research by Ghiselli suggests that hydroxyl radicals are involved in the pathogenesis of late complications in diabetes.

Catechol is a minor metabolite of hydroxyl radical attack upon salicylic acid. Its generation involves the release of a molecule of carbon dioxide. Catechol is thought to correlate with 2,3-DHB as an additional indicator of oxidative stress.29,30

Clinical Therapeutics for Oxidative Stress

In the 1970s, Pauling discussed the use of therapeutic doses of vitamin C to prevent and treat viral infections. Cathcart reported in numerous clinical instances therapeutic benefit of using "bowel tolerance" doses of vitamin C (the oral dose which will initiate diarrhea) for the treatment of many virus-related disorders.31

Although his theories have not been proven through detailed mechanistic studies, many clinicians have reported anecdotally that their patients have benefited from this therapeutic approach.

There is emerging recognition that individual antioxidants may not have as wide-ranging clinical benefits as the intake of balanced antioxidants which incorporate all the dietary redox-active substances people have consumed for millennia. This is due in part to the involvement by different antioxidants in the process of regenerating each other.

Specific antioxidants include ascorbate, carotenoids and tocopherols, but also extend into other phytonutrients such as phenols, flavonoids, and quinoids. There is growing acceptance among scientific and medical communities that enhanced antioxidant intake in the diet and specific application of antioxidants in certain states of oxidative stress may provide both preventive and therapeutic advantage.32

Related Tests

Because oxidative stress attacks the body at the cellular level, virtually every part is affected by free radical damage. The relationship of the liver and its pivotal role in detoxification leads most practitioners to order the companion test, the Detoxification Profile.

Among others, the Amino Acids Analysis looks at levels of cysteine and taurine. Low levels of cysteine (the rate-limiting factor for the synthesis of GSH) can result from impairments in methionine metabolism, made evident by the results of the analysis. Taurine is an important scavenger of the hypochlorite ion (OCI), which contributes to oxidative stress and inflammation.

Still other tests may be useful to the clinician. Recent toxic exposure and cumulative exposure over time can be assessed by Elemental Analysis of hair, urine, or blood. The test also examines levels of nutrient elements for excesses and deficiencies which can interfere with antioxidant activity in the body.

The key to effective antioxidant supplement is absorption, and suspected problems with digestion and absorption should be investigated with tests of gastrointestinal function.

The Comprehensive Digestive Stool Analysis (CDSA) is the place to start, because its results and test commentary present a useful picture of total gut environment health. The Interpretive Guidelines for the CDSA will suggest additional digestive testing, such as Intestinal Permeability Assessment and Bacterial Overgrowth of the Small Intestine, if deemed necessary. Malabsorption of antioxidant and detoxifying nutrients and increased intestinal permeability to toxins can result in an overload to the liver’s detoxication capacity.

Because nearly every modern diet is deficient in essential fatty acids, especially W-3 fatty acids, the Essential and Metabolic Fatty Acids Analysis can be instrumental in establishing a foundation for improved antioxidant utilization. Proper balance of fatty acids is necessary for effective cell communication, creating precursors for hormones, reducing inflammation throughout the body, and healthy neurological development. The interaction of metabolic mediators can be improved by restoring homeostasis of fatty acids.

Inflammation and nutrient insufficiencies, as well as disordered methionine metabolism, ultimately increase cardiac risk by elevating levels of the amino acid homocysteine and creating an environment where the C-reactive protein is called into action in response to injury and infection. Both metabolites are biochemical markers in the Comprehensive Cardiovascular Assessment, and their elevation has been associated with cardiovascular illness.

CFS and Oxidative Stress

Impaired detoxification by the liver can lead to oxidative damage of mitochondria--the principal energy source for the cells within your body. Because of this, oxidation has been cited as a fundamental mechanism in the development of CFS.1

Oxidative damage is often triggered by free radicals--structurally unstable cells that potentially damage other healthy cells in the body. That's why excess free radical activity is linked to premature aging, illness, and numerous diseases. Physiological data from animal studies has confirmed that free radical scavengers-- which limit damage from oxidative stress--significantly reduce the development of muscle fatigue.2

The Oxidative Stress Analysis evaluates the body's oxidative stress and antioxidant potential. Used in conjunction with the Detoxification Profile, this test can provide a comprehensive analysis of the relationship between oxidative stress and liver detoxification function.

Related Information: CFS and Detoxification

References:
1 Bland JS. Oxidants and Antioxidants in Clinical Medicine: Past, Present, and Future Potential. J Nutr Environ Med 1995;5:255-80.
2 Supinksi G, Nethery D, Stofan D, DiMarco A. Effect of free radical scavengers on diaphragmatic fatigue. Am J Resipir Crit Care Med 1997;155(2):622-9.

http://www.gsdl.com/assessments/oxidativestress/

Aloha Jackie,

Thanks once again for passing on this wealth of information from the A4M Conference in Las Vegas.
It just so happens I picked up some SAM-e (s-adenosylmethionine) from Costco yesterday.

Mike,

Perhaps SAM-e would be a good way to get more glutathione onboard.
Although I can see the point in most of the posts on the BB in response to your vitamin/supplement query, I certainly believe in them. Like Wil Schuemann I experienced an objective improvement in symptoms. Unfortunately detectable long lasting effects on cardiac health were not among them, except for significantly lower BP. But to each his own.

Richard,

I must thank you once again. Your earlier advice to always wear something under the hula skirt during hula lessons has served me quite well.

Mahalo

PC

From Jackie's first post above:

"Intake of white cabbage was strongly associated with an increase in rheumatoid factor-positive disease." Wow, and I thought cabbage was real good for ya! I guess green curly cabbage must also be implicated as well as white cabbage per se?

From Hans' last post above:

"1. Taking glutathione orally is a waste of time and money as it does not increase blood levels of glutathione (1)." I guess this statement lies at the heart of PC's comment:

"Perhaps SAM-e would be a good way to get more glutathione onboard."

Thanks for the excellent and informative posts Jackie, and also thanks to the Hula-King for his response regarding SAMe.

Jackie/anyone: are you aware of any studies which show whether or not, and if so to what extent, GERD remedies such as prilosec and nexium compromise/interfere with absorption of antioxidants from food and/or supplements??

A pleasure to be amongst you guys here.

No booze for me this year so far: if I do relent, it will only be the occasional glass or three per week. And I've lost almost a stone since Christmas - albeit aided in part by a nasty dose of flu over the holiday period. But hey, every cloud has a silver lining (-:

Mike F.

Here's an interesting version on CRP, the marker for inflammation, and the role of inflammation....it all goes together.

C-REACTIVE PROTEIN, a Coronary Trojan HorseBy Aftab J. Ahmed, Ph.D. Chest pain migrating to the arm and shoulder, chest pounding, dizziness and unsteadiness on the legs are symptoms of an incipient heart attack. While in a certain percentage of people these symptoms can precipitate a coronary episode, in others a heart attack may creep up unnoticed.

Research over the years has provided penetrating insights into the major causes of heart disease. Thus numerous hypotheses and models have been proposed as to what causes heart disease. The pathological triggers range from high cholesterol and triglyceride levels, obesity, high blood pressure, adult-onset diabetes and among others, chronic viral and bacterial infections.

While each of these triggers is a distinct risk factor, the basic mechanisms and their correlation with clinical presentation are only cursorily elucidated. A raft of recent reports, however, has begun to unravel the mystery behind a clogged artery or occurrence of fulminant and fatal heart attacks. In fact, the understanding of the causes of coronary artery disease is being reconsidered in light of these studies.'

The most intriguing observation, which promises to reshape our thinking about heart disease, is that the bodies defense system becomes the villain. The natural defense mechanisms ordinarily protect the body from harm and eventual diseased state. The turncoat mechanism responsible for the onset of many chronic diseases is inflammation.

An increasing amount of data suggests that inflammation may well be at the core of coronary artery disease (CAD) as well.

Typically a heart attack is thought to result from decades long, repetitive cycles of inflammation, injury, repair and reinjury on the inside of the blood vessel.2 Each cycle of injury, despite natural healing, exacts a stiff toll in the long run. Over an extended period of time the injuries cannot be healed and the damage keeps compounding.

Since prevention Of CAD is the Holy Grail of cardiovascular research and clinical practice, development of any therapeutic approach necessitates that a basic question first be answered, namely, how do injury-repair cycles affect the coronary- A coronary is gradually narrowed as the so called fibrous plaque builds up due to, as has been colorfully described, sludge in the pipes," which ultimately closes the artery. The more an artery is narrowed, the greater the risk of a heart attack. Scientists and clinicians have traditionally sought to understand what makes plaques rupture and to find ways to identify and treat them before they actually do. Buildup of the fibrous plaque is not an isolated event, however, and has metabolic consequences. As the plaques gradually take hold, at the first sign of their build up the body's immune system launches an inflammatory response.

To appreciate how inflammation could potentially precipitate a cardiac event, a brief overview of plaque formation is in order. Longstanding data suggest that CAD begins at very early stages of life with the formation of a fatty streak, which is deposition of fat in the arteries. While fatty streak is a common occurrence in a vast majority of individuals, only a percentage of them will develop CAD. This bespeaks contribution by other factors that lead to pathogenesis. In case of an initial irritation that causes inflammation in the lining of the arterial wall (the endothelium), the immune system is activated and sends its foot soldiers to the rescue. In the case of isolated irritations, after the injury heals the immune system pacifies and no irreversible damage is done. Over the course of time, however, if the endothelium is repeatedly injured, the inflammation becomes chronic.

Repeated irritation to the endothelium produces cell adhesion molecules (CAms). In the healthy tissue the purpose of these 11 sticky' molecules is to conscript the cellular repair machinery to begin the healing process. In the cardiovascular network, however, they become the proverbial pot of honey to attract the flies of cholesterol and are eventually covered by a protein coat, called the fibrous cap.

Most of the plaques develop over decades and serve as landfills for cholesterol. As the plaques mature they may occupy as much as 70 percent of the blood vessel volume, seriously restricting blood flow, and may cause angina. These plaques, however, stabilize and pose slim risk of rupture. Inasmuch as mature plaques in the long run are detrimental to heart health, it is the younger plaques, on their way to maturity, which are potential time bombs and leave considerable damage and suffering in their wake.

These younger plaques are softer and are covered by thinner fibrous caps and contain a rich lode of cholesterol. They could be likened to lava percolating under the mountain cap long before the volcanic eruption. Even though they occupy a mere 30 to 30 percent of artery volume, they are potentially volatile. These young plaques cause no symptoms since the vessel wall can accommodate them by expanding outward. Consequently they go unnoticed in angiograms.

Younger plaques, however, are like land mines that can explode by ever so small a trigger. Thus when they fatigue and rupture, sudden and massive clots can occur throughout the artery, causing a fatal heart attack. Again inflammation figures prominently here. The bodies repair mechanisms do clear cholesterol from the lining of the arterial wall. Specifically, macrophages suction off cholesterol deposits. If the plaque is rich in fatty material, macrophages gorge on it until fully loaded.

Laden thus with cholesterol, they burst open and die. As dying macrophages rupture, their cell sap is released under the fibrous cap into the bulk of the plaque. This cellular debris contains proteins that practically chew up the fibrous cap and destabilize it. In turn, the destabilized plaque becomes vulnerable to other events that raise blood pressure locally to cause it to swell and break open. To make matters worse, macrophages release a protein called tissue factor, which increases the likelihood of blood to clot and triggers fatal heart attacks.

This sequence of events is of particular interest since it encapsulates the natural history of CAD. That is, the basic processes are already in motion long before the symptoms become manifest. This forces the question that if

inflammation is indeed the underlying mechanism that contributes to heart disease, what is the lever to use this correlation in its diagnosis?

It has been known for some time that elevated levels of C-reactive protein (CRP) are found in individuals who suffer from heart attacks or unstable angina and is a garden-variety marker of inflammation.

What is CRP, though, and what is its role- C-reactive protein is an acute-phase protein produced in the liver as a defense mechanism to a wide range of stimuli. It circulates at fairly low concentrations in healthy individuals and its amounts are dramatically increased in the presence of infection, inflammation and cellular injury, such as the common cold, bacterial infection and rheumatoid arthritis.

In fact, CRP is being increasingly used in clinical settings as a part of diagnostic regimen to monitor the progression of disease and treatment results. More recently CRP has been used in predicting the risk of diseases in apparently healthy individuals, including CAD. In fact, several studies have convincingly shown that increase in CRP levels correlates with the risk of heart disease.

In the March 23, 2000, issue of the New England Journal of Medicine, Ridker et al. extended their previous work on the correlation of CRP levels to CAD and reported that CRP was the most reliable predictor.3 They evaluated several other pro-inflammatory predictors, including interleukin-6 (IL-6), homocysteine, total cholesterol, low-density lipoprotein ("bad" cholesterol) and among others, the sticky cell adhesion molecules. Combined with their previous work, the findings of Ridker et al. strongly corroborate the role of chronic inflammation in the onset of CAD.3

This work provides corroboration of the more widely known response-to-injury hypothesis. While CRP is an indicator, albeit a powerful one, of an impending adverse cardiac event, it is not per se a causative factor in CAD. It does, however, serve as a warning signal and could contribute to aggravate the deleterious effects of a causative factor in CAD. Furthermore, the Ridker et al. study does not imply that other risk factors such as cholesterol, high blood pressure, homocysteine, unhealthy dietary habits, or sedentary lifestyle, would not cause CAD.

These various factors may contribute, concurrently or sequentially, in clinical presentation of CAD. The major import of inflammation as an indicator, though, is that it may point to identification of treatment targets. It underscores the evolving opinion that more long-term benefits may be garnered as much by investigating causes of arterial injury as by the body's healing response.

What therapeutic approaches could potentially emerge from the study of inflammation in CAD- Several mechanisms may link incipient heart disease with increased levels of CRP. Thus expression of tumor necrosis factor-alpha may be increased, which can stimulate the production of CRP and can, concomitantly, inhibit the ability of macrophages to travel to the injury site. In addition, serum concentrations of IL-6 may be raised.5 This suggests that reduction of inflammatory response is of central importance in prevention of heart attacks.

The correlation of CRP with cardiac episodes promises to open up entirely new areas of research. Nonetheless, a natural remedy to manage chronic inflammation already may be available in systemic enzymes. Combination of enzymes including bromelain, papain, trypsin and proteins suchlike-have been shown to effectively reduce chronic inflammation.6

Additionally, systemic enzymes reduce levels of circulating cytokines IL-6 and tumor necrosis factor-alpha and CAMs. More important, however, are the findings reported in European studies demonstrating that an aggressive regimen of systemic enzymes may lower the amounts of CRp.7

As such, systemic enzymes over protracted periods of time may be a preventive measure in the management of CAD. Chronic, systemic inflammation has begun to be recognized as the Trojan horse of most of the age-related diseases.

There is a good reason that this would be so. Inasmuch as the immune system protects the body it is constantly switched on and off to fend against the deleterious effects of metabolic attrition. It is plausible that the body is in a constant state of alert, which can induce subclinical autoimmunity, that is, when the body turns on itself, this autoimmunity may well be the underlying cause of many of the age-related degenerative diseases.

A better understanding of inflammation, hence, is imperative in developing viable therapeutic and corrective nutritional approaches in the management of chronic conditions.

Jackie

Whoa, guys! Too much information!
Listen, I hate to play the philistine, but could somebody just explain - in simple language - what kind of supplementation would be good to lower cell inflammation, as I'm sure that's how it feels with me when I'm triggering.

I know the conference room is for in-depth discussion, but I'm really interested in this subject but, frankly, my eyes get crossed going through all this stuff. (I'm one of those who can't read computer manuals either!....but I can set it to music!!)

David

Whilst REALLY appreciating all the great work by both PC and Jackie in particular as regards input to this topic of discussion, I do - as I often do when reading about supplementation - like David get a bit bogged down as regards what to take with what etc. etc. Indeed I voiced as such in a recent post to the forum.

Now Jackie, I mean this with the greatest of respect, but having wondered this for some time, I just gotta ask you, how many different supplements do you take each day, and at what $ cost per month?? I don't in any way enjoy pointing this out, but after many years of the most dedicated and determined and well-intended research, you did actually in the final analysis opt for a surgical procedure to finally and (I'm most glad to observe) successfully address your own AF. OK, assuming that one has some semblance as to what one is actually doing, I appreciate that ones' health is WELL worth forking out for, but I really do - like David - struggle with the whole supplementation issue. Whilst I appreciate that the big pharmaceutical groups are in it for the bucks, I also see plenty of evidence that the producers of alternative 'neutraceutical' products are also in the game for the same reason. Supplements are a growing bandwagon, and I personally see no reason whatsoever to be any less wary as to the prime motivating force behind the production and marketing of supplements than I am pharmaceutical products as prescribed by docs. At the end of the day, bombarding ones' body with ANYTHING other than natural good quality and preferably organic food should surely be undertaken with caution. In nature's scheme of things, we are inextricably interwoven as an organism with the food we eat as the result of a many thousand year old relationship, and a well-balanced diet has an deep and subtle balance which one could never hope to achieve with supplementation. Furthermore, my mind is as I write darting around thinking that maybe an intracellular Mg level of 40 units for me is as appropriate as a level of 60 units for you Jackie (range 40-60 for argument's sake).... we are, after all, as a chap on the forum oft used to point out, all just experiments of one. Sooooo much to try and get one's head round.... as is always the way with life.

Rant over,

Mike F.

Hi again PC,

Another question for you (hope you don't mind the questions!) regarding pole or pacemaker cells this time.

As I understand it, afibbers have extra pole cells in their left atrium and pulmonary veins. I have always been wondering why we have extra pole cells and when did they first develop in the heart. Is it hereditary or as most of us have developed afib in our 40's was there some environmental trigger or maybe too much stimulus to the vagus nerve re: GERD, inflammation or something, that caused the brain or heart to respond by producing extra pole cells to these chaotic signals?

Hope this makes sense.

Dean

Dean,

My understanding is that post mortem examination of cardiac and pulmonary tissues shows that ALL the general population have the extra pole cells. THe Q accordingly is.. why does the presence of the same result in AF for some and not for others?? If I've got this wrong in broad terms, maybe PC will leap in to keep us all on the right track.

Mike F.

Hi Mike,

In the March 2004 AFIB Report Hans reported an article from the Cleveland Clinic stating that P cells, normally found only in nodal tissue (SA node, AV node), were found in 5/5 with AF and in 0/5 controls without AF.

I'm surmising that this alone is not enough to elicit AF, otherwise we would have had it from birth. That's where the oxidative stress comes in with clinical expression of AF only after many years.

PC

PC,

Thanks for that clarification: left me wondering whether AFrs have had the extra PV-located P-cells from birth, or whether they kinda accumulate/increase as we age?? I wonder, in fact, whether or not oxidisation itself might ironically actually increase the number of P-cells in the PVs?? If those rogue P-cells (in Pvs) ARE there from birth, then for such folks (like us) it's rather a matter of 'when' than 'if', with the oxidisation issues merely bringing the 'when' on at an earlier stage.

Jackie,

Thanks for sharing your viewpoint. I wonder if I might trouble you for some further advice and input. As you know, I'm in the UK, and the only place I can find in the UK which does extensive testing on a non-NHS basis (i.e. I pay for it privately) is an outfit called BioLab whose Internet address is
http://www.biolab.co.uk/tests.html

Would you please have a look to see whether in your not-inexpert opinion they offer anything like the intracellular function testing to which you allude in your above post? If you think they offer anything which it might be in my best interest to pursue, then I'm up for it. Come to that, given my history of chronic childhood stress, anxiety, OCD, GERD, and ectopy etc. what tests would you get done by BioLab if you were me? I know I'm only 43, but I want to look after myself the best I can in the future. My NHS doc sure isn't interested in getting me any additional testing doen: e.g., my ferritin is 345 but he ain't interested in getting me any more iron-related blood work done. He says to take no notice of the fact that all the info on the Internet says that ferritin should preferably not be over 50 cos all lab ranges are different and the one used for my ferritin test has an upper range of 480. FWIW, I think the medical docs here in the UK in the main are more into placating patients with pharmaceutical symptom control rather than proper health screening and preventative measures.

Respect to you Jackie,

Mike F.

Mike - I will check out that URL - give me some time... I'll get on it this afternoon and get back to you.

I'd just like to comment that if you are concerned about a high ferritin level... I presume it is high - but I realize our measures could be different from yours but the high number looks "high" regardless of the standard....

why not just go and donate blood. Tell them you have to much iron and want to get rid of that. They can dispose of the blood or use it for plasma content (I think)... you can do this every six weeks and get the numbers down...while you are investigating how to test and equate the numbers.

Here in the US, the recommended approach - at least with the people I know who have hemochromatosis - is just to have a blood draw every month or six weeks until the correct number is reached.

David - Pure and simple.... antioxidants and anti-inflammatories to reduce inflammation....

vitamin C, vitamin E, selenium, highly effective is alpha lipoic acid....
I mentioned in another post, N-acetyl cysteine is the ultimate antioxidant and of course, Omega 3 fish oils.

Other supplements that are highly anti-inflammatory.... PCO - (proanthocyanidins), ginger, bromelain, turmeric.

There is a very good anti-inflammatory product by Wobenzyme (German company) called Wobenzym N.... highly effective to reduce C-reactive protein. It is a combination of enzymes and bioflavonoids.

The critical measure of levels of inflammation is the test for the marker is CRP.... This along with Homocysteine, Ferritin and Fibrinogen should be tested (blood draws) and monitored on a regular basis for progress.

Dosages are going to be different for each individual. This is where the testing comes in. Check progress on a regular basis by blood draws.

So - first be tested and then plan which antioxidants/anti-inflammatories you'll begin with... monitor results with more labs.

I am totally convinced that a large portion of what brings on AF is the result of irritation (inflammation) of the P cells as PC has pointed out here... and it will happen randomly to those who have inflammation from oxidative stress in the area of the P cells which are irritated or inflamed in the area of the pulmonary veins. High levels of HDL in the area of the PV is contributory to inflammation.

I think the second major factor in AF is essential electrolyte deficiencies of both magnesium and potassium.

Jackie

Mike - I've looked at the website for the tests and note you could certainly spend quite a bit out-of-pocket on these tests, but the problem is, you really need a doctor to at least speculate what might lie at the bottom of some of your symptoms. Otherwise, the question becomes where to begin.

I've had to pay for many of my cellular profiles out of pocket as well. I just felt it was something I needed to do since the standard tests wouldn't address the nutritional deficiency. Just as we know serum magnesium isn't a true picture of intracellular status.

Remember... the key markers for staying out of trouble...
C-reactive protein - marker for inflammation and atherosclerosis
Homocysteine - also involved with inflamm. and athero.
Fibrinogen - too much means too much blood viscosity - clotting tendency
Ferritin - we've covered this one
Also fasting glucose and insulin to make sure you don't have a glucose handling problem.

Perhaps you can correspond with this lab to determine which, if any of their tests, would offer you indications for these markers.

I don't see much they way they have them labeled, but I'm not very conversant with various labs.

They do have a Homocysteine profile.... that would be a start

Serum B12 is good to consider since you've had the stomach problems, you may not be metabolizing what you need in the way of B12 for homocysteine and the methylation issue. The problem would be who would help treat you if there was an abnormality. As you say, your doctor doesn't seem too interested in prevention.

You've already addressed the uric acid situation, I believe, but for overall health and heart health, especially, those four markers plus the blood lipid profile is just pretty standard or basic.

I emphasize with your medical situation and what they consider adequate health care delivery insofar as prevention is concerned. Many people here in the US have a medical plan called an HMO and some plans do not want to do any of the basic preventive diagnostics because their goal is to keep costs down...not help patients stay well...or even prevent a future problem. I know of two cases where prostate cancer should have been addressed early on but was glossed over for 18 months and by then, it was too late for these patients. Criminal.

I don't think I've been of much help here.... But since you know your ferritin is way too high...at least if your scale is equal to ours, consider the blood donation route at the very least.

Then I'd ask about the CRP and definitely go for the Homocysteine.
Keekp me posted of what transpires.

I honor your decision to do as much as you can to improve your health while you are young enough for your efforts to make a real difference. Everyone should be as mindful as you are. Good job, Mike.

Be well,
Jackie

Hi Mike,

Regarding your question about oxidizing agents causing the production of more P cells, I'd say no.

Up or down regulation of ion channels has been well described. However, actual change in cell type is more difficult for me to swallow. Furthermore, oxidation should damage the cell not change it from a Cadillac to a Ford.

Just my opinion.

PC

Thanks very much for the further info and opinions Jackie.

My last CRP was - in the words of my Doc - "under 4 and that's really low" He couldn't tell me more and said the lab he uses never give the actual figure, just a kind of pronouncement.....

As regards Homocysteine, I had it done recently ($140-00) and the result was 9.5. Not brilliant, but not THAT high as such either.

I imagine that my predisposition towards gout will elevate my CRP as will any GERD issues. I'm not sure if the same goes for Homocysteine or not.

As regards ferritin, I'm actually scheduled to give blood tomorrow!

Thanks again,

Mike F.

The article, **Atrial Fibrillation: Are We Treating the Right Disease**?, in PC's first post brought up nitric acid and oxidative stress. The following book might have some insights as to how to train and minimize the oxidative damage.

Body, Mind, and Sport : The Mind-Body Guide to Lifelong Health, Fitness, and Your Personal Best by John Douillard, Chapters 10-15. John, an ex pro-triathlete, addresses stress and training. He has developed an exercise technique that minimizes stress, but ultimately allows for a high level of physical output, but at a low metabolic rate. He is creating a vagal state during exercise. This has never bothered my afib, even though I'm vagal. I suppose this is because I'm exercising, the balance is still away from the vagal. It is very interesting. He also addresses how nasal breathing increases nitric oxide formation and absorption over mouth breathing.

Here is the short version of his approach (I've added web links to explain part of this. John has full explanations in the book):

1. Sun Salutation (http://www.abc-of-yoga.com/yogapractice/sunsalutation.asp) with Darth Vadar breathing (Ujjayi Pranayama, closed glottis only on the exhale - see end of post) through the nose. Inhale when expanding, exhale when contracting. Three rounds (one half round is shown on the web site - go through one complete side then back through as a mirror image). A minimum of 5 seconds on each pose.

2. Start exercising very slowly, continuing Darth Vadar nasal breathing. Keep very slow for 10 to 15 minutes.

3. Now start increasing your pace, continuing Darth Vadar nasal breathing. Listen to your body. If you feel the least bit of fatigue, or if you have to open your mouth, back off your pace. For many days, this will be a limit for you. Some day you may be able to increase your output, without feeling any fatigue. Generally, your output will increase, but your heart rate and breath rate will stay constant.

The punch line. In a study John conducted, group of athletes tested at the same resistance (200 watts) on an exercise bicycle on two different days, with and without this technique - 47 breaths per minute without, 14 breaths per minute with. A man who took up running in his late 30's was going to give it up because of breakdown problems. Then he took John's class. After training using John's techniques for 18 months, he was able to run 17 miles at a 6 minute/mile pace. His heart rate averaged 120 and his breath rate 12 to 15 breaths per minute.

John also addresses nitric oxide and nose breathing. He quotes a Japanese Journal of Physiology study (I don't have the exact reference - I have old version of book, nitric oxide quotes are in new version & I just copied those pages from library book w/o references) found that nasal passages produced a significantly higher amount of nitric oxide than mouth breathing did. This study also found that at least 50 percent of nitric oxide found in exhaled air was produced in the nasal passages. Another study, by the American Physiological Society found that nitric oxide is not only produced in the nose, but adsorbed there as well. This study indicated that if we exercise with nasal breathing and increase nitric oxide then we will be better able to absorb and utilize its benefits.

An approach such as this might minimize oxidative stress on the system during exercise. I took a class from John about 10 or 12 years ago. I quit running and started walking at an 11 to 12 minute/mile pace. I don't always use his technique, but if I don't, I work out at a low heart rate. I only violate this a couple of times a year (like entering a race up Pikes Peak). I think this has served me well - I stay in good condition, but don't have a lot of stress issues from doing so. For example, today I was walking at an 11 minute/mile pace and my HR was 125.

George VMAF 49

Ujjayi Pranayama (Darth Vader breathing) http://www.yogabasics.com/pranayama/UjjayiPranayama.html
is called the ocean sounding breath because you make an ocean sound by contracting the glottis with the inhalation and exhalation. This Pranayama is done through the nose, but it is helpful to begin practicing breathing through the mouth. To make the ocean sound, whisper the syllable "h," feeling the contraction in your throat. Keep this contraction engaged on the inhalation and exhalation. After a couple of breaths try to close the mouth, breathing through the nose while still making the ocean sound in your throat.

Hi George,

I'll have to try that on my next run. I don't usually count my respirations, but I'll give it a go.

PC

Mike - I just wish we had an understanding or a correlation of US lab test ranges and what you might be using there in the UK.... then I'd feel better about the numbers you are mentioning.

For us here... CRP - Reference range: .00 - .50 mg/dl… with ideal being as close to zero as possible.
Your under 4 number scares me...but then, I don't know how this compares to our ranges.

Same thing for the Homocysteine....

Cardiologist, Stephen Sinatra says “Generally, “normal” for homocysteine is anything between 5 and 15 micromoles per liter, but epidemiological evidence suggests that optimal levels are less than 8 mm/l.

Population studies in the Mediterranean Basin (France and Spain) have low mortality from cardiovascular disease, with levels averaging 7 –8 mm/l.

In countries with high mortality rates (Finland Scotland, Northern Ireland, Germany) homocysteine levels average 10 – 11 mm/l.

He considers anything above 9 to be dangerous.” (Sinatra Health Report 3/01)

Yes - true...you're not that "high" but my doctor is happy when my numbers are 6 or less. This all has to do with methylation and it's work to change the numbers...so forewarned is forearmed.

One of holistic doctors speaking on atherosclerosis...this is the danger from the CRP and HCY elevations....says it's high time we start treating the blood to get rid of this problem before it starts becoming an atherosclerotic plaque problem. Prevention is where it's "at."

I'm glad to see you are giving blood. That's a powerful step in the right direction, Mike. Good for you.

Be well,
Jackie

Jackie,

Thanks again for the info and input.

I think the units for my CRP are mg/l. Therefore 'less than 4' as stated by my GP translates to less than 0.40mg/dl (I'm assuming that there are 10 dl to a litre). If so, things aren't too bad, hence my doc's view that my levels are low.

Re. HCY levels, mine was 9 when last measured thus putting me right in between the Mediterranean and Scottish et al good and bad camps as it were. So, work to do there then. I wish I could remember what Richard used to say as regards knowing whether one is a good or a bad methylator.....

Cheers,

Mike F.

Dean,

The impression I'm getting is inflammation and pacing of cells go together, it's just that we as afibbers get to experience it first hand. The following is not a good example but :

http://www.painonline.com/mt-archives/2004/07/long_term_poten.html

Now what is strange is the ability of small injuries to become, as it were, a pacemaker, which alters the frequency of the oscillations. The term pacemaker has traditionally been reserved for a small area in the right atrium of the heart. This area acts as a sink for electrical activity generated by the heart muscle cells. When the current gathers, it collects at the spot in the atrium which has the LOWEST firing frequency. In some ways this may mean the tissue there is the most excitable since current excites it and is then dispersed until a new signal is generated from the natural activity of atrial muscle. What is important to remember is that if the pacemaker is injured, some other area of the atrium will become the pacemaker. This OTHER pacemaker will ALWAYS fire at a rate faster than the natural one.

This bears repeating. An unnatural pacemaker always fires FASTER than the healthy, natural one. With this model in mind, let us move back to the brain. Should a small tumor or even an encysted parasite occupy an area of the brain, seizures frequently occur, which may march across the ENTIRE brain. How can such a small area interfere with the DISPERSAL of brain signal which ordinarily permits varied and discrete functions to operate simultaneously in the brain. There is a weakness in the synaptic complexity of the brain. The interconnections of the brain mean that it is theoretically possible for any ONE neuron to connect or send signal to ANY OTHER NEURON. Since there are at least six thousand synapses per neuron, the resulting number of permutations and combinations of synaptic connections is mathematically greater than the number of atoms in the known universe. So how does one little area of damage, one little tumor, cause seizures. The answer is that is abnormal tissue and draws signal together, defeating dispersal. Dispersal is essential to conscious, normal brain function. Processes blocking dispersal create abnormal results. McHenry has postulated that failure of dispersal in the oscillations of thalamic relays of the VPL/VPM nuclei leads to excitability in the cortex, which leads to pain.

Angus

Hi Mike - I wasn't ignoring your post - I just haven't been back to the CR after posting those other lengthy gems.

I do spend a huge amount of money on supplements. The reason is I had so many conditions that weren't getting better. One by one, they have been resolved. The doctor I see, as I have mentioned previously, is a functional medicine MD. She tests to see what nutrients are missing from specific cellular functions...and then prescribed "targeted nutrients" to fix the problem.

Don't forget, Mike, I'm 68 and considerably older than you are...and so as we age, we become deficient from a variety of means. The conditions that I've been able to normalize so far are, hypoglycemia, insulin resistance, hypoadrenalism, hypothyroidism, fibromyalgia, chronic fatigue, candida overgrowth, GERD, and of course, AF. I still have the multiple chemical sensitivity issue and I doubt if that will ever be resolved.

Yes, I did opt for ablation and this was an executive decision on my part. I felt I needed to do that because my excellent insurance was in jeopardy of coming to an end and I wanted to be sure I had the procedure covered.

Currently, I'm cutting way back on many supplements because I no longer need them .... and I'll be tested routinely to see if I can hold on my own through nutrients in food, or if I will have to revert back to supplementation.

I know after attending the Anti-aging Convention, those of us who are near or over 60.... absolutely must supplement and I've addressed those key issues in the notes from the forum.

It truly isn't confusing when you have the intracellular function testing that targets every system to see if a key element is missing. In one case, I was not methylating correctly and in spite of the supplements I was using, my Homocysteine was still higher than it should be. I began then to have B12 injections and the whole thing turned around. Without testing, there is no way to do this without stabbing in the dark or the shot-gun approach. I feel fortunate to be able to have access to this doctor and the benefit from her knowledge of biochemical nutrition so that I can live well in my senior or "golden" years as we like to say here.

My criteria is...I want to feel well, function well, love life, be active, look young and healthy and take no prescription drugs. So far, I'm managing to accomplish that quite well.

Before I went down this nutritional supplementation path, I felt like I was on the path to my early demise .... AF was just one of the problems.

Hopefully, I'll continue to improve. So far, so good.

Be well, Live with Passion.

Jackie
