Dr. Rath Health Foundation Alliance Talk

July 9, 2013 – John Cha

Hello. Today we are going to take a look at some of the lesser known benefits of dietary vitamin C. You are well aware of dietary vitamin C's importance as an antioxidant, its critical function in collagen synthesis, the reliance of the immune system on vitamin C, and also the importance of vitamin C in preventing atherosclerosis and cancer. However, some of the more obscure facets of vitamin C benefits may not have been revealed, even to academic scientists and medical practitioners of the conventional establishment. We'll highlight some of these interactions as it relates to homeostatic mechanisms or the way the body maintains balance, the structural function of the heart, the structural function of the kidney, and some recent evidence of its ability to stave off environmental damage, including our very own in house results. As time goes on, the evidence from independent research only corroborates what Dr. Rath and Dr. Pauling had to say about additional dietary vitamin C as a critical foundation for improved health. From this mutation of vitamin C synthesis evolved a few key genetic adaptations in humans, of special note which is Lipoprotein(a), and an additional mutation that occurred after the vitamin C mutation, the uricase mutation. These later mutations compensated for the loss of vitamin C.

In an ongoing process, our flesh and bones frames for our consciousness have adapted in ways that it could, surviving prior mutations by exploiting new ones. These same mutations that at one point in time helped humans survive also are our vulnerabilities. Take for example, the high vulnerability of humans to heart disease compared to other vitamin C generating animals. Other omnivores and carnivores that generate their own vitamin C do not develop atherosclerosis throughout their natural lives in a way that mimics human pathology. Even forcing them to exhibit human atherosclerosis requires extraordinary and unusual diets or chemical stimuli. Apo(a) appears, uricase disappears, and other adaptations occur in its place, yet these genetic adaptations were never fully able to restore and rescue the genetic defect for vitamin C synthesis. Despite all our advances in technology and knowledge, humans are still vulnerable to the very simple absence of a substance from citrus, a vegetal extract, vitamin C. As proud and intellectual a creature as we have become, the human frame still succumbs to scurvy today in 2013, just the same as it did thousands of years ago. We still die within days without water, within minutes without air. So then we return to and revisit our biochemical and evolutionary vulnerabilities in a scientific capacity and ask the uniquely human question of "Why Vitamin C?"

Well, then why Vitamin C? Scientists have long speculated why we lost the ability to generate our own vitamin C, but no one has settled on one story or the other. They do know why we need it, and why we need it in levels beyond simply preventing scurvy, which is the last overt manifestation of vitamin C deficiency before death follows. Health is more than preventing death, it is about pushing all parameters of health to their fullest functional potentials, not a minimal level just enough to prevent dying. Scientists only relatively recently stumbled upon a genetic error that we in fact do not share with the majority of animals, and that they do not incur our major mechanical vulnerability, heart disease.

This extended to so many other facets of well-being that our investigations into vitamin C have generated as many new questions as answers. It is not an exaggeration to state this. Only now have the first clinical trials of intravenous vitamin C in cancer patients begun in people by the conventional establishment after so many years of skepticism and worse. The most recent academic answers to many old long-standing questions regarding vitamin C and health have been a definitive, "Yes it is so." With this, we'll begin with the first slide of my presentation, "Vitamin C Does A Body Good."

2 Vitamin C Not Just For Sailors

It is essential for everyone, no matter how well they may think they will fare without it. Those who are under more physical and psychological demands and exposed to more noxious stimuli of any kind will need more.

3 New Biochemical Interactions of Vitamin C Discovered in 2013

Many new functions of vitamin C have been revealed recently and some speculative functions of vitamin C have been confirmed. Like a master key that unlocks all doors, vitamin C regulates many different actions in the body that must work in concert with one another for proper function.

4 Data Excerpt From: L.A. Da Costa et al./Journal of Nutritional Biochemistry 24 (2013) 842-847
"Association between the plasma proteome and serum ascorbic acid concentrations in humans"

In this comprehensive study of the blood levels of many proteins in thousands of individuals, the authors divided people by tertile of vitamin C blood level. The lowest category, or "tertile" was people with levels of vitamin C under 23 micromoles per Liter of blood. The second highest category, or "tertile" was people with levels of vitamin C between 23-36 micromoles per liter of blood. The highest tertile was designated as people with more than 36 micromoles of vitamin C per liter of blood. In fact, these tertiles which are arbitrary designations were set on the low end, with the preferable concentration of vitamin C being at least 50 micromoles per liter of blood. However, we see a very fine regulation between these vitamin C levels and these various proteins. The more vitamin C present, the less of these proteins. The statistical significance which is greater with a lower number is quite high for these figures. There is not a precipitous drop in these blood proteins which would also indicate a disease condition, but a parallel fall in the proteins with vitamin C rise in the blood. Why this is good or bad will be discussed 2 slides later.

5 Practical Impact

The blood proteins that decrease with increasing vitamin C levels all have important normal functions, but are elevated in various disease conditions. When vitamin C increases, these disease conditions also decrease and with them, the disease associated elevations in these proteins. Knowing this, a person would consume as much vitamin C as is optimal for them to prevent these disease associated elevations. Also, knowing this, it would be counterproductive to do the opposite, consume as little vitamin C as possible, as then the disease associated proteins would increase.

6 Functions of Proteins Listed

While these proteins have normal functions, they are elevated in various diseases and acute phase reactions to injuries and inflammatory conditions. Their levels indicate health or disorder in the blood. The key importance is not too much and not too little of these proteins, which vitamin C assists in maintaining.

7 Vitamin C Attenuates Acute Phase Reactant Responses Beneficially

An acute phase reactant is a protein that is manufactured in response to injury to participate in limiting or repairing the damage. Some of these are called positive and go up in response to a certain condition, and others are called negative because they go down in response to a certain condition. When this system is unresponsive or dysfunctional, the positive reactants may go up at the wrong time or not go up at the right time. Likewise in a deranged acute phase response system, the negative reactants may fail to decrease as they should or be increased instead. Together with Dr. Roomi, we designed and executed a study examining the effects of vitamin C deprivation, vitamin C supplementation, and vitamin C with other nutrient supplementation upon the acute phase reaction to a well studied inflammatory chemical, turpentine oil. We found that the presence of vitamin C was associated with a precise and appropriate reaction to the turpentine oil and that nutritional mixtures containing vitamin C (Epiquercican) had an augmented effect compared to vitamin C alone. Scurvy had a damaging effect in causing inappropriate increases or lack of response to the chemical inflammatory insult by various acute phase reactant proteins.

8 Vitamin C Benefits In The Inflammatory Response

This flowchart describes the experiment conducted in Gulo (-/-) mice, which can't produce their own vitamin C like normal mice. Two groups of mice with 3 subsets were begun on the same regimen of a vitamin C absent diet for 2 weeks in order to synchronize their blood levels of vitamin C levels to minimal levels. These are marked blue. One sub-group was left to continue for another 2 weeks on scurvy diets, while another subgroup was returned to a vitamin C equivalency to 0.5% Epiquercian diet marked green, and the third subgroup resumed on 0.5% Epiquercican fortified diet. After the total of 4 weeks, one half of the mice were injected with turpentine oil in the hind limb muscle. After 24 hours, the blood was studied for changes in acute phase reactant proteins.

9 Dietary Vitamin C Promotes Appropriate Acute Phase Reactant Responses
(Stand Down or Act As Required)

This graph displays the differential response to turpentine oil by various proteins between non-injected and injected mice. Scurvy mice had much more Lipocalin induction compared to Vitamin C or EQC supplemented mice, blue, red, and green, respectively. Lipocalin-1 participates in sequestering iron from pathogens and is seen in kidney disease. We see the same pattern in Pentraxin-3 involved in the immune response, and Haptoglobin, which participates in destroying hemoglobin and making iron unavailable. Of great interest and novelty was a much reduced increase in Alpha-2-Macroglobulin in scorbutic mice, as compared to vitamin C supplemented mice, and an even higher response in EQC supplemented mice. The significance of this will be explained next.

10 What is “Alpha-2-Macroglobulin (A2M)?”

Alpha-2-Macroglobulin prevents collagen breakdown and the tissue damage that would occur from it. Normally present in the human blood as a kind of dampening protein to prevent collateral damage from normal protein cutting enzyme activity, the levels of this protein rise as an acute phase protein, possibly to prevent the breakdown of newly formed blood clots or to halt chain reactions of collagen destruction from plasmin activated collagenase enzymes.

11 Alpha-2-Macroglobulin Inhibits Plasmin, Which Activates Collagenases

Plasmin, which is involved in breaking down blood clots also activates collagen degrading enzymes. By inhibiting the activity of plasmin, Alpha-2-macroglobulin prevents the excessive destruction of collagen.

12 What Does The Above Mean To A Human? *Vitamin C Promotes Balanced Function*.

13 For Lungs: Vitamin C Protects Guinea Pigs Exposed to Cigarette Smoke

Guinea Pigs like humans do not generate their own vitamin C and will develop a kind of atherosclerotic lesion in response to vitamin C deficiency. In an experiment in which researchers subjected Guinea Pigs to cigarette smoke in a smoking chamber, higher vitamin C levels were definitively protective to lung tissue. This is a very practical day to day application which has tangible protective benefits.

14 Dramatic Real Benefits of Vitamin C in Protection of Lungs from Cigarette Smoke

In a graph taken from the paper, “Cellular and molecular mechanisms of cigarette smoke-induced lung damage and prevention by vitamin C” by Banerjee et. al., we can see very clearly the effect of vitamin C deficiency on reducing lung resistance to cigarette smoke. While the top line of guinea pigs do not suffer an enormous breakdown of lung tissue after 3 weeks of just 1 milligram of vitamin C without smoking, the second line of guinea pigs suffer a gradual but eventually massive breakdown of the lung architecture. The amount of smoke administered was from 5 cigarettes per day. We see lung architecture literally dissolving away, leaving large voids where lung used to be after 3 weeks of cigarette smoke and only 1 milligram of vitamin C per day. The third line of guinea pigs are amply supplemented with 15 mg of vitamin C a day and has more surface area and active lung surface than either the 1 mg/day guinea pigs or the 1mg/day guinea pigs with cigarette smoke. The fourth line of guinea pigs subjected to 5 cigarettes per day while on 15 milligrams per day of vitamin C exhibit significantly less breakdown of lung tissue. The difference is obvious to the untrained eye, which demonstrates that the effect is not small.

15 Kidneys

Most people are not aware that collagen serves a critical function in the kidney. In fact, without collagen, the kidney’s evolutionary design would not work at all. There are various disorders in which collagen may over accumulate in response to chronic injury and disease, which may be referred to in order to suggest that collagen is “bad” for the kidney. However, in collagenous breakdown disorders in

which the kidney is involved, the kidney fails outright. Of course, we know that without ample supplies of vitamin C, there cannot be correctly formed collagen in the kidney or anywhere else in the body.

16 Vitamin C Deficiency Known To Cause "Leaky" Kidneys

It is more than conjecture; it is already proven that vitamin C has a direct and essential role in kidney function. Just as capillaries, arteries, and connective tissues of the body loosen, weaken, and suffer holes without vitamin C, so do kidneys which become "leaky" without vitamin C. Here we see a graph of a scurvy patient's amino acid re-uptake by the kidneys before and after vitamin C treatment. After 4 weeks of vitamin C supplementation, the kidneys stop leaking amino acids into the urine.

17 Vitamin C Deficiency Known to Cause Less Blood Flow Through Kidneys (Less Filtration)

Vitamin C deficiency not only causes kidneys to become leaky, but also reduces their effectiveness. Without blood flow through the kidneys, there cannot be blood filtration. Vitamin C deficiency causes a definitive reduction in several parameters of kidney function.

18 Collagen Essential to Kidney Function

Renal collagen is a less known, but a well-studied component of the filters of the kidneys. In addition to nephrotic syndromes from collagen breakdown from chronic disease, there is the well-known athletic nephritis. In athletic nephritis, a temporary leakiness of kidneys to protein occurs in response to strenuous exercise which subsides after rest. Just as in the coronary arteries, the tremendous increases in blood flow and pressure through the kidney can cause temporary ruptures of the collagen filtration membranes which are quickly repaired under the presence of optimal vitamin C levels. Without collagen, the kidney's selective function is defeated, and without vitamin C, there is no collagen. The importance of vitamin C to kidney health may currently be overlooked and underestimated.

19 Filtration Barrier In Kidney

Here we have a graphic depiction of the complex barrier structure of the kidney's filter membrane in the glomerulus. A membrane of collagen and laminin sits between heparan sulfate, creating a functional charge and size cutoff filter which allows only particles smaller than 8 nanometers of neutral to positive charge through. For example, normally albumin does not pass through but water, sodium, and potassium do.

20 The Kidney Stones Myth

Even the conventional medical establishment admits to themselves that there is no evidence that additional vitamin C causes kidney stones as this is rarely a causal association. It is understood that high urine pH is associated with calcium oxalate or phosphate stones, that persistently acidic urine is associated with uric acid stones, infection with struvite stones, and a genetic order to cystine stones. (http://www.kidney.niddk.nih.gov/kudiseases/pubs/kidneystonediet/)

21 Vitamin C Deficiency Directly Damages the Heart, In Addition to Its Arteries

It may be less well understood that there is collagen inside the heart wall itself. In various structures inside the heart chambers and inside the heart wall, there are kinetic structures whose function would be severely compromised by collagen degradation. In fact, collagen is not just critical to good arteries, but a good heart. For example, it is found in the "Trabeculae carneae."

22 Without collagen, these important pieces of your heart would fall apart, and the muscle cells would float away.

Imagine that with every pump of the heart, this structure is held together by collagen and other extracellular matrix components. Without this tensile strength, the whole structure comes apart at the seams with each component failing to work as a coherent team of cells as they all float away in their own individual directions. Collagen failure means functional failure of several parts of the heart itself.

23 Dilated Cardiomyopathy (Heart Failure)

In a particularly devastating heart disease, the walls of the heart gradually become thinner and larger, until the original shape of the heart which is important to its mechanical function becomes a large balloon shape. The diseased heart has trouble pumping and delivering the same amount of blood as it did previously. This is yet another disorder in which collagen degeneration has a direct involvement in the progression of the disease yet is not widely recognized as a collagen degeneration disorder.

24 Degenerative Cascade of Functional Collagen Degradation Followed By Aberrant Collagen Replacement Occurs in Dilated Cardiomyopathy

Many academic laboratories have studied whether collagen degradation in the progression of Dilated Cardiomyopathy occurs. In fact it does and the collagen turnover processes found in other body systems participate in the degenerative remodeling of the heart as well. A destructive cascade occurs in which excessive conditions may damage both the cells and the collagen fibers, causing both degradation of good collagen, the death of working cells, and the replacement of both by a malfunctional collagen subtype. There are several subtypes of collagen with specific functions and normal locations. In last resort conditions, as in DCM when heart cells and functional collagen are being destroyed faster than they can be repaired, the remaining cells lay down aberrant collagen. The cycle continues so long as the damage occurs, eventually building the malfunctional balloon shaped heart which is preferable to wall destruction and outright hemorrhage.

25 The Heart Muscle Cell Collagen Matrix

Here we see the fine structure of the bundles of contracting motor cells of the heart or myocytes as they are bound and sheathed together with collagen. The electron microscopy shows the abundant rope or strand like filaments of collagen about the cardiomyocyte architecture.

26 Chordae Tendineae are 80% collagen, and the remainder consists of endothelial cells and elastin. Without these "heart strings" your 1-way valves would open the wrong way, causing severe pressure drops.

These tendon like structures which serve to keep the valves opening in only one direction are mostly collagen. Without optimal vitamin C levels, these are in danger of damage and malfunction too by virtue of collagen degradation.

27 What Happens When The Collagen Cables in the "Chordae Tendineae Cordis" Break?

The chordae tendineae are subject to the same processes of collagen dissolution as all the other tissue in the body. When these are inappropriately activated near the valve, and the collagen ruptures, mitral valve prolapse, a debilitating condition occurs.

28 Is Vitamin C Beneficial *In Vivo* For Congestive Heart Failure In Paced Rabbits*?*

In this study, the authors electrically over-worked rabbit hearts to pump at 360 beats per minute and compared the results of a vitamin mix that contained vitamin C, no vitamins, or just alpha-tocopherol at preventing heart failure. The results were impressive, taking into account that no synthetic drugs were applied but only a vitamin mixture containing vitamin C which was superior in benefit to just alpha-tocopherol alone. The biochemical response of the human heart and the rabbit heart is similar enough to appreciate the implication that B-carotene, vitamin C, and alpha-tocopherol in combination might have a benefit in prevention of human heart failure.

29 Explore the Heart @ www.bodyxq.com

Explore the heart as it pumps in real time! You can teach yourself about the heart with this free educational application.

30 Not So Subtle Effects from Loss of The Vitamin C Gene

When this group studied the changes in genes between mice that had a working copy of the vitamin C synthesis gene and mice that had it deleted (Gulo (-/-), they found that antioxidant genes were affected negatively, with important antioxidants systems being depressed. Some others were upregulated in an attempt to redundantly compensate for Superoxide Dismutase, and Glutathione Peroxidase, but these compensatory changes do not represent full restoration of antioxidant function. The take home message here is that the loss of the vitamin C synthesis gene also had a negative impact on the antioxidant genes that remained.

31 Gulo (-/-) Defect + Uricase KO in Humans Naturally Inclines Them to Convert Fructose to Fat

A little known mutation that occurred after the loss of the vitamin C synthesis gene was the loss of the uricase gene function. This causes humans to accumulate uric acid, or urate, not to be confused with urea. Scientists postulate that this was a compensatory adaptation to the loss of vitamin C, as urate is a sort of poor man's substitute for vitamin C antioxidant function. Uric acid also causes fructose to be stored as fat more efficiently as well as induces hypertension. How these effects of uric acid could be beneficial at the time is examined in the next slides.

32 Later Uricase Defect That Countered Gulo (-/-) Defect in Humans Naturally Inclines Them to Hypertension (High Blood Pressure)

As a human being without vitamin C synthesis and faced with old fallen fruit to eat before the winter, one would eat it and eat it in vast quantity before it vanished. Unfortunately, this is the time when vitamin C levels in fruits also drops while fructose increases. It may have helped humans survive by storing as much fructose as possible as fat, and without uric acid this is difficult to do as the fructose does not as readily become fat. Additionally, as an upright walking person, one would want to keep walking to the next food source, shelter, or run away from a threat despite having low salt levels. One would not want to faint because of low blood pressure, but to maintain it even under low salt and food levels. Urate does precisely this, raise blood pressure. At the time, hypertension could have been a great survival advantage. There are also other speculations that urate protected the brain and so forth while vitamin C synthesis remained defective in humans.

33 Dietary Vitamin C Combats Effects of Uricase Knockout Too

A pivotal study published in 1989 in the Bruce Ames laboratory compared the rate of consumption and also the potency of various physiological antioxidant substances against lipid peroxidation, a fancy word for "fat rusting" which when occurs causes functional lipids such as that contained in LDL to become rancid. They found that while uric acid was the last to disappear, it also could not protect lipids from oxidative damage. Ascorbate was the first to vanish, and it was also the only antioxidant that could afford protection against peroxidation of lipids. Urate simply cannot substitute for ascorbate antioxidant function, but ascorbate can. Additionally, elevated urate is associated with increased cardiovascular disease, which is an additional flaw and drawback of urate as an antioxidant. Ascorbate is known to reduce blood pressure rather than raise it, antagonizing the hypertensive quality of urate. Additionally, ascorbate can prevent high blood pressure caused by fructose.

(Dietary vitamin E and C supplementation prevents fructose induced hypertension in rats. Mol Cell Biochem. 2002 Dec;241(1-2):107-14.)

While some new groups have found that 500mg a day of supplemental vitamin C did not reduce uric acid, previously other groups did find it to reduce urate. The low dosage is probably responsible for the disparity of results between human trials in which multi-gram daily doses might have shown a more pronounced effect. More importantly, ascorbate is able to eliminate the damaging qualities of urate by working with it to scavenge other types of damaging free-radicals such as byproducts of peroxynitrite and urate. This information can be found in the paper by Kuzkaya et. al. "Interactions of peroxynitrite with uric acid in the presence of ascorbate and thiols: implications for uncoupling endothelial nitric oxide synthase." in the journal Biochemical Pharmacology Volume 70, Issue 3, 1 August 2005, Pages 343–354 (Biochem Pharmacol. 2005 Aug 1;70(3):343-54.) In effect, by scavenging the free-radicals caused by urate, urate can serve as a sacrificial antioxidant rather than a net sum free-radical source.

34 Our Old Biochemical Evolutionary Adaptations Are Also Our Current Biochemical Vulnerabilities

35 Vitamin C Does A Body Good

Please visit http://www4.dr-rath-foundation.org/ where you will find out about all this and more.