Metabolic Cardiology

The ‘Awesome Foursome’ – Protecting Healthy Hearts, Restoring Ailing Hearts

by Stephen T. Sinatra, MD, FAAC, FACN

Over the years, I’ve treated countless cardiac emergencies, people literally a heartbeat away from death. I’ve done middle-of-the-night heroics and slept in hospital beds next to critical patients. Early on in my career, I came to the conclusion that I wasn’t really healing anybody. I duly followed what I had been taught, applying the drugs and techniques du jour aimed at directly “fixing the problem”; and, for the short term, those efforts worked. However, I gradually realized that I often treated the same people over and over without really getting them well. It was a revolving door.

Early on, I also developed a keen interest in the bioenergetics of the heart. Such a statement may seem strange to you, but the fact is that cardiologists aren’t trained to think in terms of nurturing the energy processes involved in the heart’s essential function as a pump.

In the 1980s, antioxidants were starting to come of age and my patients were asking me about them. So I began reading up. I wanted at least to be able to answer their questions when they inquired about safety and effectiveness. Would antioxidants interfere with the drugs that doctors relied on? Were they dangerous? Could high doses be dangerous? What about side effects? It took time to find all that out.

At first, I became comfortable with familiar minerals like magnesium and calcium for their heart-healthy benefits. Then vitamins E and C, and other mainstream antioxidants. The research papers about nutritional supplements kept piling up on my desk for me to read when I had a chance.

Around that time one of my favorite patients, a 50-year-old minister, needed valve replacement surgery, the result of ruptured chordae tendineae caused by voluminous mitral valve prolapse leaflets. His heart was otherwise normal. The coronary arteries clinically clean. The surgery at a nearby hospital was a success, but the surgeons couldn’t wean him off cardiopulmonary bypass (the heart-lung machine). Every attempt failed. It went on for hours. He couldn’t live without the pump. Eventually, their attempts failed.

I cried when I heard the news. I believed that there must have been something I could have done to prevent such a tragic death in the midst of the best technology and surgeons available. I searched my “to read” pile on my desk and saw an article in a 1982 issue of the Annals of Thoracic Surgery recommending a nutrient I knew nothing about – called CoQ10 – that helped people come off the heart-lung bypass machine after open-heart surgery. You can imagine how bad I felt. I couldn’t help my friend, but from then on I began telling patients awaiting open-heart surgeries to start taking CoQ10 daily two weeks ahead of their operation. Every patient subsequently who used CoQ10 came off the heart-lung bypass machine without a problem. In a sense, the death of one patient helped save the lives of others.

The tragedy of a lost patient accelerated a personal mission to learn as much about nutrition and nutritional supplements as I could. Thanks to that process, I have been able to rescue many disabled and ailing hearts, even the sickest of them. I’ve been able to give patients the wherewithal to make remarkable comebacks and extend the quantity and quality of their lives. Nutritional medicine can do that so remarkably.

CoQ10 to the Rescue

One case I’ll never forget happened in 1996. I received a desperate phone call from a man trying to save his dying, hospitalized mother, Louise. She had heart failure, and six specialists had given up on her and recommended discontinuing life support. The son, a biochemist, had pleaded with the doctors to give his mother CoQ10, and had even brought them supporting medical literature. They refused, saying it was not on their list of approved medications. The son went to the hospital administrators. They said he was interfering with accepted hospital practice.

The man begged me to take his mother as a patient even though it meant a risky, hour-long ambulance ride to the hospital where I was working. I agreed. Upon her arrival, I immediately placed the semicomatose woman on conventional pulmonary
Two weeks, she was able to sit in a wheelchair with only supplemental oxygen, and the hospital discharged her to an extended care facility.

I continued to work with Louise, putting her on a combined program of medication and broad nutritional support. She followed the recommendations to the letter and later moved home, where she lived a good, self-sufficient life for another seven years before passing away as the result of a different medical condition.

Louise was a true medical resurrection — one that demonstrates the great life-saving and life-extending potential of nutritional intervention.

Since Louise's time, I have enlarged my nutritional arsenal. The results have been so dramatically positive that I wrote a book about it: The Sinatra Solution: Metabolic Cardiology (Basic Health Publications). At the core of metabolic cardiology and so many other great patient comebacks are CoQ10 and three other supplements I collectively call my "awesome foursome." The other three are carnitine, magnesium, and D-ribose.

To be sure, I also recommend a high-quality multivitamin and mineral, plus vitamin C, fish oil, and other important nutraceuticals; but these four are my big cardiac weapons.

The awesome foursome are nothing less than awesome for the prevention and treatment of cardiovascular disease — from arterial disease to heart failure. Each of these compounds — available as nutritional supplements — represents a necessary raw material used by the mitochondria, the power plants within cells, to produce adenosine triphosphate (ATP), the fuel that drives the cellular machinery, which in turn keeps the heart and all the other systems of the body running. In my experience, the awesome foursome is the best way to target and feed the heart's energy needs. Individually and collectively they increase ATP production.

Energy-guzzling heart muscle cells require large amounts of ATP to contract and relax, maintain cellular ion balance, and synthesize macromolecules like proteins and fats. Your body generates ATP de novo as well as recycles it through a process called oxidative phosphorylation. A much faster process than synthesizing ATP from scratch, recycling is the preferred method of energy production. Eighty to ninety percent of ATP is recycled in the mitochondria, then released into the fluid portion of the cell to be used for energy.

Mitochondria require each of the awesome foursome to generate ATP. While CoQ10 and L-carnitine are fundamental to the ATP recycling process, D-ribose is necessary for de novo ATP synthesis. Metaphorically, D-ribose helps fill the body's gas tank, while CoQ10 and L-carnitine help the body convert fuel to energy. Like a spark plug central to both processes, magnesium "turns on" the enzymes that drive the entire metabolic reaction.

Depending on the individual, supplementation with any or all of the awesome foursome may be the key to maintaining energy and overall health. At around age 40, endogenous production of CoQ10 and carnitine generally starts to decrease, explaining why lack of energy is commonly associated with being "middle aged."

People with heart disease often have CoQ10, L-carnitine, D-ribose, and/or magnesium deficiencies. Standard medications often create or exacerbate such deficiencies; the most notable example is interference with CoQ10 production by cholesterol-lowering statin drugs. A person suffering from coronary artery disease (CAD) will likely require supplementation to meet his or her energy demands. The presence of CAD requires the heart to continually overwork in order to pump blood through inflamed and congested blood vessels. Ultimately, the organ expends energy much faster than the mitochondria can produce it.

Deficiency is also the largely undiagnosed — and unaddressed — source of diastolic dysfunction. Energy declines because of a shortfall of the energy substrates that generate ATP. Diastolic dysfunction may develop one or two decades before the evidence of systolic dysfunction, which then typically leads to congestive heart failure.

Awesome Foursome in Action

Following is a brief rundown on the roles of these important compounds as well as my recommended daily dosages.

CoQ10

Co-enzyme Q10 is a vitaminlike substance synthesized in the body. Production declines with age and poor diet, and is significantly impaired by statins. The current medical obsession with cholesterol and the use of statins as a pharmacologic prevention strategy are, in my (as well as other integrative cardiologists') opinion, a formula for long-term disaster and may be an underlying cause for the sharp increase in the incidence of heart failure.

Inside our cells, electrons are extracted from the food we eat to make ATP. CoQ10 molecules perform a central role in that process by shuttling electrons back and forth between enzymes.

CoQ10 is also a formidable free-radical scavenger — a property that makes it doubly essential because ATP production is accompanied by profuse free radical activity. CoQ10 also protects cellular membranes and components, as well as arterial tissue, from free-radical damage that generates inflammation and leads to disease and accelerated aging.

CoQ10 is a key ingredient for healing all cardiovascular conditions as well as helping prevent energy loss associated with aging. For patients with heart failure, it is life-saving because their hearts are starving for energy.
Commercial CoQ10 supplements vary in potency. Look for a supplement bioavailable enough to therapeutically raise CoQ10 levels in the blood. Bioavailability describes how quickly, and in what concentration, substances are absorbed by the blood. Water- and fat-soluble forms tend to be more bioavailable than dry powder blends. Blood levels provide the most accurate assessment of how much CoQ10 is being absorbed and delivered to tissues. Researchers agree that a 2.5 μg/ml blood level of CoQ10 is optimal, while 3.5 μg/ml is the preferred amount to help heal severely diseased hearts. I have not yet seen any advantage to using the newly developed ubiquinol form of reduced CoQ10 over ubiquinone.

**Dosage:** 90–250 mg per day for the prevention of cardiovascular and periodontal disease; 180–360 mg per day for those with hypertension; 300–600 mg per day for heart failure.

### Carnitine

Carnitine is a water-soluble amino-acid-like compound present primarily in meat. The body endogenously produces L-carnitine with the help of two amino acids (lysine and methionine), as well as vitamins C and B6, iron, and niacin. To avoid carnitine deficiency, vegetarians should supplement and/or combine such foods as beans and rice, which contain lysine and methionine, respectively.

Carnitine performs an exclusive mitochondrial transportation role. It ferries fatty acids to be oxidized to make ATP. Keep in mind that the heart obtains 60% of its fuel from fat sources, so it is highly dependent on L-carnitine. Equally important, this compound carries waste material out of the mitochondria, such as toxic metabolites that could otherwise disturb the burning of fats and cause disruption inside of cells.

Oral L-carnitine is poorly absorbed. Because of this, I suggest ingesting it in smaller doses three times per day on an empty stomach.

**Dosage:** There are several forms of carnitine, including L-carnitine, acetyl-L-carnitine, and glycine propionyl-carnitine. My preference is a broad-spectrum supplement that includes these subtypes. Take 1,000–1,500 mg in divided dosages to prevent deficiency, and up to 3,000 mg for individuals with heart disease.

### Magnesium

Inside cells, the biggest magnesium concentration is found in the mitochondria. All enzymatic reactions involving ATP have an absolute requirement for magnesium. In addition, magnesium is a contributing partner for more than 300 enzymatic systems in the body.

People get magnesium through diet, drinking water, and/or supplements. We don’t produce it in the body. Abundant in leafy green vegetables such as kelp and spinach, magnesium is also found in almonds, cashews, pumpkin seeds, beans, tofu, figs, apricots, and bananas. Mineral-rich hard drinking water contains magnesium. Softened or bottled water usually doesn’t. Since soil is becoming increasingly magnesium deficient, and cooking and processing also leach magnesium from foods, supplementation in conjunction with a healthy diet is the way to go.

Magnesium is highly beneficial for treating angina, arrhythmia, atrial fibrillation, atherosclerosis, strokes, heart failure, heart attack, high blood pressure, and mitral valve prolapse. As a muscle relaxant within arterial walls, it alleviates chest pain and other symptoms of angina due to lack of oxygen to, or energy in, the heart. Taken regularly, magnesium can help maintain vascular tone and healthy blood pressure, and may also contribute to reversing arterial plaques. Magnesium also helps prevent insulin resistance.

Magnesium deficiency is very common. Chronic emotional and physical stress deplete magnesium. In angina, there is a direct correlation between deficiency and frequency of chest pain. Various bowel diseases and some GI medications, such as histamine 2 antagonists, may impair absorption of dietary and supplemental magnesium. Long-term diuretic therapy, commonly prescribed to treat high blood pressure, is another problem. It drains the body of many important minerals, including magnesium. Supplementation is essential for anyone on such a program. I have had many new patients whose regular doctors put them on diuretics tell me that they were experiencing dementia, memory loss, cramping, and fatigue. I only use diuretics for a short period of time to avoid mineral depletion.

Blood tests alone are insufficient to determine a real magnesium deficiency and deficit in tissues. Sixty-five percent of magnesium is present in the mineral phase of bone and 34% is sequestered in muscle, leaving only 1% residing in plasma and interstitial fluids. Although a mononuclear blood level analysis can better predict magnesium deficiency, physicians should investigate patients’ dietary histories to see if they consume enough leafy green vegetables and fruits, especially if mitral valve prolapse, ischemic heart disease, heart failure, or hypertension are at issue.

**Dosage:** The only contraindication for magnesium is kidney failure or insufficiency or situations where hearts already beat at a slow rate, at less than 60 beats per minute. Loose stools are the only common side effect of excess magnesium consumption. Just cut back. Chelated forms of magnesium, such as glycinate, taurinate, and orotate, are best absorbed. Australian researchers have found that magnesium orotate may be the best for promoting ATP. Take at least 400 mg.

### D-Ribose

D-ribose is a naturally occurring sugar derivative of ATP. Under certain cardiac conditions – especially during ischemic episodes like angina and...
heart attack when the heart is deprived of oxygen – there’s a profound depression of ATP. Individuals with ischemia have low levels of ribose, which compromises the heart’s ability to resynthesize and regenerate ATP. A drop in ATP means a subsequent plummet in myocardial function, and the heart struggles to pump.

Whether one needs to supplement with ribose depends on one’s lifestyle and health condition. Generally, the body makes enough ribose in tissues like the heart, skeletal muscle, nerves, and the brain to meet its daily metabolic needs. However, people whose cells and tissues are oxygen depleted, or because of illness are otherwise metabolically challenged, may be deficient in ribose. Their energy demands exceed what their bodies can produce. Thus those with ischemic heart disease, heart failure, hypertension, fibromyalgia, and chronic fatigue syndrome, along with serious athletes, need to supplement with ribose.

Oxygen deprivation, which characterizes ischemic heart disease, forces the body to make energy through a means other than oxidative phosphorylation. To survive, the body will switch to glycolysis, or glucose metabolism, a much less metabolically efficient, albeit very important, process that provides the body large amounts of energy in short bursts. The problem with glycolysis replacing oxidative phosphorylation is that it will cause exhaustion over time. The body, no longer able to recycle ATP, will also become unable to synthesize it de novo, as the glucose that it would have reserved for ribose synthesis is eventually used for fuel.

Ribose supplementation in these situations is a great energy booster for the heart. It bypasses the need for ribose synthesis, a slow process that must be accomplished before ATP synthesis can begin. In other words, supplementing with ribose helps regenerate energy much faster.

Ribose is quickly and easily absorbed through the gut into the blood. The amount of supplemental ribose needed depends on the presence of chronic oxygen depletion or circulatory problems. Ischemic blood flow can result in delayed ribose delivery and higher doses are recommended.

**Dosage**: 5–7 g daily as a preventative for cardiovascular disease, for athletes on maintenance, and healthy people doing strenuous activity; 7–10 g daily for heart failure, other forms of ischemic disease, peripheral vascular disease, patients recovering from surgery, and athletes participating in regular high-intensity exercise; 10–15 g daily for those with awaiting a heart transplant or with heart failure, dilated cardiomyopathy, frequent angina, fibromyalgia, or neuromuscular disease. Take in divided doses.

**The Awesome Foursome and Medication**

Patients taking pharmaceutical drugs for cardiovascular disease may need to supplement to prevent nutrient deficiency and subsequent unpleasant side effects. Beta blockers, for example, effectively stabilize patients in emergency situations and improve symptoms, but they inhibit the production of enzymes necessary for CoQ10 synthesis. Statins, as mentioned earlier, are also CoQ10 antagonists. Since long-term use can impair a person’s ability to make ATP, adjunctive supplementation with CoQ10 can counteract pharmaceutical side effects associated with energy depletion.

In a Nutshell

A healthy ATP energy pool may be the fountain of youth. While you can’t take ATP as a pill or vitamin, you can give the body the next best thing: the raw materials to make ATP. Supplementing with the awesome foursome helps boost ATP production and significantly improve health to both prevent and treat cardiovascular disease. Not only can such supplementation ameliorate various symptoms, it can improve the underlying pathology. Targeting nutrition at the cellular level in this manner significantly improves outcomes across the board.

Stephen Sinatra is a board-certified cardiologist and certified psychotherapist with more than thirty years of experience in helping patients prevent and reverse heart disease. He is also certified in anti-aging medicine and nutrition. Dr. Sinatra is a fellow of the American College of Cardiology, an assistant clinical professor of medicine at the University of Connecticut School of Medicine, and a former chief of cardiology and medical education at Manchester (Connecticut) Memorial Hospital. His numerous books include Reverse Heart Disease Now (Wiley; 2008) and Earthing: The Most Important Health Discovery Ever? (Basic Health Publications; 2010). He is also author of the popular nationally distributed newsletter Heart, Health & Nutrition and host of the drsinatra.com website.