

Metabolic Cardiology-

It's All About ATP - Part 2

An Interview with
Dr. Stephen T. Sinatra, M.D., F.A.C.C.



By Richard A. Passwater, Ph.D.

Last month we chatted with Dr. Stephen Sinatra about new nutrients to keep the heart and arteries healthy, particularly a nutrient called propionyl-L-carnitine (PLC). This month, we will focus on metabolic cardiology and how adenosine triphosphate (ATP), and thus its precursors, the carnitines, CoQ-10 and D-ribose, is the bottom line in heart health. Anybody with any type of cardiovascular disease has a heart that is always leaking ATP. The body can't make it back fast enough by *de novo* (from the beginning) synthesis! It takes too long and the *ATP leakage* is faster. It's all about ATP and less about oxygen!

Cardiologists are always thinking about oxygen in the heart—and oxygen is important—but oxygen is only the stepping-stone to ATP. Oxygen is only a tool—but a vital one—in the production of energy via ATP. But, it is not the oxygen that provides the energy of life—it's the ATP. "Life" depends on the body utilizing energy to drive the vital biochemical reactions of life. In the "living" process, "free energy" is needed to power reactions that otherwise would not occur. The chemicals would just sit there, unreacted. The Energy needed to cause the chemicals is obtained from the release of chemically stored energy. Energy is a force, not a compound. The principle source of "free energy" in the body is a special high-energy phosphate group (high-energy bond phosphate).

In order for "life" to occur, or for muscles to move and perform mechanical work or exercise, or for the heart to beat, "free energy" must be liberated through a chemical reaction where ATP is split into adenosine diphosphate (ADP) and the high-energy bond phosphate group (the source of free energy).

In previous chats with Dr. Sinatra, we have discussed the emerging field of metabolic cardiology and how it is saving lives and improving the quality of life in heart patients. Metabolic cardiology is a sub-specialty of cardiology that deals with the very core of heart disease itself—the biochemical changes in cardiac cells by which energy is provided for vital processes and activities.

Actually, metabolic cardiology is more than energizing and powering the heart because the same factors energize and power all of the cells in the body. Metabolic cardiology applies to preventing and overcoming fibromyalgia, chronic fatigue and Syndrome X, just as it does to all aspects of heart disease.

In the introduction to Dr. Sinatra's new book, *The Sinatra Solution* (Basic Health 2005) cardiologist Dr. Jim Roberts points out several shortcomings of conventional cardiology and how it was missing the boat in terms of not being able to stop the continual decline in heart func-

tion even after arteries had been stented or by-passed and proper medications given. Why didn't wall motion return to normal? Why was there a functional delay in recovery?

Dr. Roberts comments, "Now we know the answer to all these questions—it is energy depletion. The ischemia ... burns off the adenine nucleotide pool, the source of cellular energy. Hibernating regions of the heart don't contract because they lack energy—they're alive, but they don't have a large enough energy supply to contract."

Stephen T. Sinatra, M.D., F.A.C.C., F.A.C.N., C.N.S., is a board-certified cardiologist and a certified bioenergetic psychotherapist, with more than 27 years of experience in helping patients prevent and reverse heart disease. He also is certified in anti-aging medicine. He is a fellow of the American College of Cardiology and former chief of cardiology at Manchester Memorial Hospital where he was director of medical education for 18 years. Dr. Sinatra is also assistant clinical professor of medicine at the University of Connecticut School of Medicine.

At his New England Heart & Longevity Center in Manchester, CT, Dr. Sinatra integrates conventional medical treatments for heart disease with complementary nutritional, anti-aging and psychological therapies that help heal the heart. He is uniquely qualified to give advice on nutritional supplements and the heart. Dr. Sinatra is one of the few medical doctors who formulates his own vitamins. He is expert in dosage, absorption, how to pick quality ingredients, and the effects of combining supplements with cardiac medications.

Dr. Sinatra has authored and/or co-authored several books on heart disease and is the editor of the monthly newsletter on heart health, *The Sinatra Health Report*. His most recent book is the aforementioned *The Sinatra Solution*. Additional information can be found on his website at www.drsinatra.com.

Passwater: *You are always at the forefront of metabolic cardiology. In previous chats, we have traced your evolution of metabolic cardiology from CoQ-10 to the "Twin Pillars of Heart Health," to the triad of CoQ-10, carnitine and D-ribose, and even to the "Awesome Foursome," which adds magnesium to the previous three. How did the evolution of your research and therapies come about?*

Sinatra: I have been using CoQ-10 for some 20 years—ever since around the time that Dr. Emile Bliznakov came out with his 1987 book *The Miracle Nutrient: Coenzyme-Q-10* in 1986. Actually, my first exposure to CoQ-10 was in 1982 when I read an article in the *Annals of Thoracic Surgery*. I have been using

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CoQ-10 in my practice since 1985 or 1986.

I have been using the carnitines for 10 years. Specifically, I used L-carnitine at first, then added acetyl-L-carnitines about five years ago. I have been aware of the role of L-carnitine in the mitochondrial turnover of ATP since the late 1980's or early 1990's. There have been many very interesting studies published on the carnitines in the cardiovascular journals since then about how heart cells deficient in carnitine and CoQ-10 cannot perform adequately.

Now an improved heart-specific carnitine called propionyl-L-carnitine (PLC) is available and my patients are gaining even more benefit.

I have been using D-ribose for about three years now. I learned about D-ribose at a meeting on aging from fellow cardiologist Dr. Jim Roberts, who wrote the introduction to my book.

Passwater: *What is the magical metabolic "Triad" for metabolic cardiology?*

Sinatra: Coenzyme Q-10, collectively carnitines (as there are three carnitines). There is L-carnitine, acetyl-L-carnitine which gets more into the brain than the heart, and there is PLC, which has a very fast half-life (the time required for the quantity to fall to half of its initial value). PLC gets inside the heart and other muscles (both peripheral muscle and carnitine muscle)—this is a very heart-selective carnitine.

Any of the carnitines will increase ATP turnover and that's why they are important in the triad of metabolic cardiology.

The third nutrient in the Triad is D-ribose, which really provides the precursor. This is the five-sided sugar that combines with adenine and three phosphate groups to make the ATP molecule.

"CoQ-10, carnitine, or D-ribose enables patients to last longer on a treadmill."

No one, to my knowledge has done a study of all three nutrients together. I want to do such a study to see if the combination synergistically results in even longer time. They are going to give people a much better quality of life and reduce a lot of human suffering.

Now, if you do a biopsy on ailing hearts, and you measure carnitine and CoQ-10 levels, they are diminished. That literature is old. Drs. G. Littaru and K. Folkers showed this about 40 years ago.

Passwater: *So as this strategy has evolved—CoQ-10 and carnitine as the "Twin Pillars"—to which you added D-ribose?*

Sinatra: Then there is the fourth nutrient, magnesium, and we have what I call the "Awesome Foursome." However, I have always used magnesium as a cardiologist even during my residency and fellowship in cardiology. So I have been using magnesium for some 30 years. Most doctors are already familiar with magnesium.

As for my involving awareness of these nutrients, carnitine and CoQ-10 were literally placed in my path. I read the literature and, as a cardiologist, I wanted to see if they would help my patients. As you know from writing your books, the best way to become very informed on a subject is to give lectures to other cardiologists wishing to know more about your treatment and then write a book on that subject. Publishers asked me to gather my lectures in a more reader-friendly format for both patients and cardiologists. Writing the books made me really appreciate the complexities of the nutrients.

One thing I did learn from writing the books and using the therapies on thousands of my patients and subscribers to my newsletter, many of whom write to tell me about their success with carnitine and CoQ-10 and the positive feedback about what these substances have done for their lives. So when you take in the literature, and use the nutrients every day in your practice, you get a flavor of how these vital nutrients are really working. Then as you learn

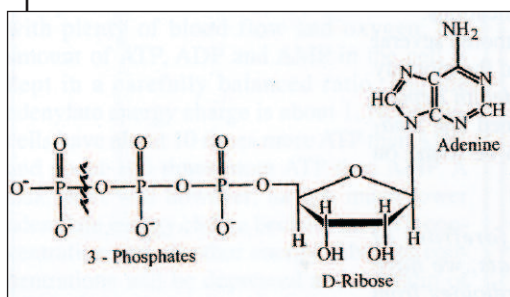
more and more about them, your comfort level increases and that why I'm really enthralled about this newest generation of carnitines.

Passwater: *You mentioned that there is quite a bit about CoQ-10 and L-carnitine in the medical literature. Yet, if I were to pick up the phone book and call every cardiologist in my area, I doubt that I would find more than one in 100 who knew anything about L-carnitine and heart disease. That's because there are no drug salesmen knocking on their doors telling them about the benefits of the carnitines. The cardiologists will be very informed about heart pharmaceuticals as they are patent-protected profitable drugs that pay for the drug companies' investment in sending out salespeople to educate the doctors. Nutrients have no such patent protection and resulting profit.*

Sinatra: Yes, this is how many, if not most, doctors receive their continuing education in this country. The pharmaceutical representative will come to the doctor's office, show him or her the results of a double-blind clinical trial, hand out some free samples, suggest that they be tried on patients and may even buy the doctor and his staff lunch, spending extended time with them to explain more intricacies about the medicine. But this is not going to happen with nutrients because of the patent issue that limits the profitability that supports this type of education.

Meanwhile, there is a glimmer of hope. The American College of Nutrition has an exam for any doctor who wants to become certified nutrition specialist (CNS). They can take this exam. I can tell you this: I am on this examination committee, and I will lobby to have these nutraceutical substances on the exam. I think they are so vital for cardiovascular and general health that they need to be included on board examinations so that physicians come to understand their vital interplay.

Passwater: *You are also invited to speak at various meetings and symposia of physicians who are also very interested in complementing their treatments with nutrients. You often speak at the educational symposia at the American College for the Advancement in Medicine (ACAM), the American Association of Anti-Aging Medicine (A4M), Expo East, Expo West, etc. Thus, you are constantly educating physicians about how to complement their practice with nutrients. Still, you, personally, can reach only a minority of those who should be learning about the benefits of these heart-healthy, artery-healthy nutrients. Your books certainly help to educate a few physicians who have open minds, but I believe that, possibly even more important, are the testimonies of your readers and patients who call their doctors to explain how CoQ-10, or*



In fact, you can take patients—I saw this written up years ago—and put them on CoQ-10 on a treadmill and you'll get about a minute longer before they experience ischemia. The same thing is true of L-carnitine, and the same thing also is true of D-ribose.

All of these studies have been done individually where you can do a crossover study, double-blind, do a washout, and all of a sudden you get a minute longer on the treadmill by using one of these nutrients.

carnitine, or D-ribose, or fish oil have helped them.

In addition to your books and newsletters, you have been kind enough to discuss these topics with us over the years. I have posted many of our chats on my website at www.drpasswater.com. I particularly would like to refer our readers to the following topics:

- CoQ-10 (Jan.-Feb. 2004) (http://www.drpasswater.com/nutrition_library/Sinatra_1.html)
- The Twin Pillars (April 2004) (http://www.drpasswater.com/nutrition_library/Sinatra_3.html)
- Soft plaque and hard plaque (Aug 2004) (http://www.drpasswater.com/nutrition_library/Sinatra_5.html)
- Real causes of heart disease inflammation, homocysteine, Ox-LDL (July 2004)
- Fish oil and arteries (2004)
- Nutrients for blood pressure (http://www.drpasswater.com/nutrition_library/Sinatra_4.html)

In addition, I have posted several articles on CoQ-10 with various researchers, including Drs. Bill Judy and Emile Bliznakov, and D-ribose with Dr. John St. Cyr (http://www.drpasswater.com/nutrition_library/John_St_Cyr.html).

Sinatra: When I lecture at these conferences—and the conferences are being attended by more and more doctors—there are now about 3,000-4,000 doctors who go to these conferences. Especially the A4M. What is very interesting is that these doctors come up to me and say with surprise, “You’re a board-certified conventional cardiologist.” Once they see that I have the same credentials that they have, they relax and listen.

In fact one cardiologist told me the other day that one of his patients gave him my book. He asked me, “What’s your background?” When I said, “Well, just like you, I sent 10 years in the Cath Lab,” he immediately became interested. Like the rest of us, doctors tend to respect people who are just like they are, and who have had the same kind of training and initiation.

I think the pendulum is starting to turn. Instead of, as you said, finding one in 100 who knows about nutritional therapies, now it might be five or 10 out of 100. And I’m optimistic that over the next five years it’s going to be maybe 50-50.

Passwater: What is the “bottom line” on metabolic cardiology?

Sinatra: I have been taking care of cardiac patients for 30 years, and I am only now beginning to realize what the bottom line might be. I didn’t realize this until I was writing my new book, *The Sinatra Solution*. As I was trying to write a clear explanation, I had this incredible “Aha!” moment. It was almost as if a light bulb

“In anyone with cardiovascular disease, the heart is always leaking ATP.”

was switched on over my head!

Here, the, is what I believe the bottom line of metabolic cardiology can be: Anybody with cardiovascular disease—I don’t care if it’s someone with a bypass or stent, or someone with hypertensive cardiovascular disease with a large left ventricular or mitrovalve prolapse or mitral regurgitation, or a diabetic with high inflammatory involvement (any or all of the above conditions where the heart is compromised in some way)—the heart is always leaking ATP!

The bottom line is that the body can’t make ATP back fast enough by *de novo* synthesis! It takes too long and the ATP leakage is faster than the replacement process.

So what I’ve learned in the cardiovascular population is that it is always playing catch up! These patients cannot get enough ATP in their cardiac cells because the ischemic or compromised heart is always leaking ATP that it is gone from the cytoplasm forever!

It is burned to uric acid and other metabolites. What I have learned as a clinical cardiologist is that it is all about ATP. It’s not about oxygen! Cardiologists are always thinking about oxygen in the heart—and oxygen is important—but oxygen is only the stepping-stone to ATP.

Passwater: Perhaps I should repeat my theme on ATP once again. “Life” depends on the body utilizing energy. In the “living” process, “free energy” is released from chemically stored energy. Energy is a force, not a compound. The principal source of “free energy” in the body is in the high-energy bond phosphate group.

In order for many thousands of biochemical reactions to occur or for muscles to move to perform mechanical work or exercise, “free energy” must be liberated through a chemical reaction where ATP is split into adenosine diphosphate (ADP) and the high-energy pyrophosphate (P) group (the source of free energy).

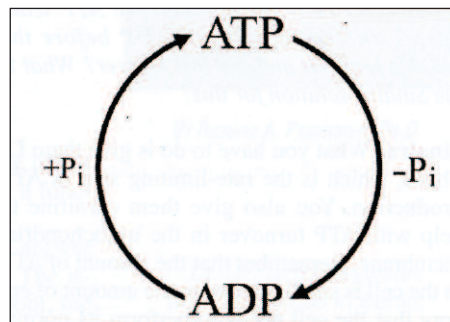
Let’s talk a little about ATP leakage since this is so important to the new understanding of metabolic cardiology.

When ATP is broken down to ADP with the energized phosphate P group being cleaved

that’s where our energy comes from. It’s that cleavage of the phosphate group.

What happens in ischemia is that the Krebs cycle (citric acid cycle) shuts down.

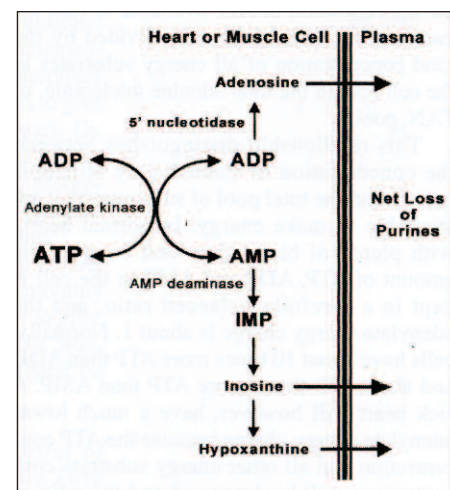
Sinatra: Yes, basically, the Krebs cycle



becomes poisoned, so to speak. Enormous levels of ADP are generated which can’t regenerate back to ATP. Then AMP is formed. With the high levels of AMP, this diffuses (leaks) out into cytoplasm of the cell. The last-ditch effort of the cell in ischemia is to form adenosine. Adenosine is like a vasodilator to keep the cell fortified with oxygen. When adenosine is released, what happens is that the vital adenine nucleotides are diffused out of the cell forever as they are degraded to uric acid and other by-products.

The figure below shows this process.

The body cannot make back the ATP fast enough. *De novo* synthesis of ATP can take



weeks—some researchers say up to 100 days (it takes a long time to make ATP by *de novo* synthesis). What I have learned about metabolic cardiology is this—there is a constant leakage of ATP in ischemia. Now remember, a lot of these patients have silent ischemia, so they don’t even know they have it. This is especially true when left ventricular hypertrophic cardiomyopathy of the heart is involved, or even in diabetes where the symptoms of ischemia go unnoticed because of diminished pain fibers associated with the diabetes.

ATP gets depleted in the cardiac cells and these patients develop enormous deficits. Fatigue and shortness of breath become major problems; angina is a problem; arrhythmia is a problem.

The task is to get them back the ATP they need.

Passwater: *How do you stop the ATP leakage? Can you recycle the ADP before the purines leak out and are lost forever? What is the Sinatra solution for this?*

Sinatra: What you have to do is give them D-ribose, which is the rate-limiting step in ATP production. You also give them carnitine to help with ATP turnover in the mitochondrial membrane. Remember that the amount of ATP in the cell is small relative to the amount of energy that the cell needs to perform its normal work; so the ATP supply must be replenished (turned over) continually to keep a constant supply of energy available.

Passwater: *How do you measure how much ATP is available in comparison to how much is needed?*

Sinatra: It would be convenient if we had an ATP gauge like cars have gasoline gauges, but we don't. However, we do have several ways in which to measure ATP availability biochemically. I prefer two systems. The first is called the adenylate energy charge. The adenylate energy charge of the cell is calculated based on the concentration of ATP available to fuel the various functions of the cell, divided by the total concentration of all energy substrates in the cell (called the total adenine nucleotide, or TAN, pool.)

This relationship distinguishes between the concentration of immediately utilizable energy and the total pool of substrates that are available to make energy. In normal hearts with plenty of blood flow and oxygen, the amount of ATP, ADP and AMP in the cell is kept in a carefully balanced ratio, and the adenylate energy charge is about 1. Normally, cells have about 10 times more ATP than ADP, and about 100 times more ATP than AMP. A sick heart will however, have a much lower adenylate energy charge because the ATP concentration and all other energy substrate concentrations will be depressed and ratio of ATP, ADP and AMP will be out of balance. Using this measurement, a healthy heart might register about 0.998 and ischemic heart might register 0.180. This is quite a difference and makes it easy to determine heart health.

A second measure of energy in cells determines the amount of energy available to actually complete all of the energy-consuming reactions of the cell. This is called the cell's chemical driving force, and it's measurement is called

the free energy of hydrolysis of ATP. The measurement of free energy of hydrolysis determines the total amount of cellular energy that is available to perform cellular work. It's akin to determining the amount of electrical energy present in a battery. Think of it like this: Measuring the amount of energy in your battery will tell you if there is enough power to start the car, turn on the headlights, and run the radio. Similarly, measuring the amount of energy in the cell determines if there's enough energy to drive contraction, ion regulation, and molecular synthesis.

Passwater: *That is indeed very interesting, but if you don't mind, I'll pass on how this measurement is made for the time being.*

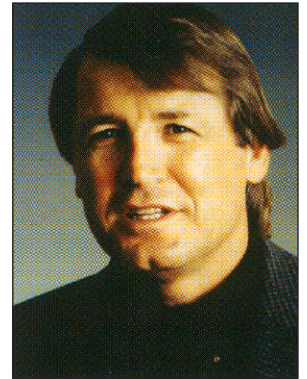
What I would like to talk about instead are some studies suggesting that creatine can help with ATP turnover in the heart. Have you worked with creatine yet?

Sinatra: There's no reason why people with compromised hearts can't use creatine. I will have to give creatine a good look as I continue to evolve metabolic cardiology and ATP production.

Passwater: *Creatine has also been shown to help with ATP recycling in the brain.*

Sinatra: Yes. Creatine is indeed of interest.

Dr. Stephen
T Sinatra,
M.D.,
F.A.C.C



Passwater: *Well, you have certainly made great strides with metabolic cardiology and the "Sinatra Solution."*

Sinatra: Thank you. Based on all of the results in the medical and scientific literature, as well as the results from my practice, carnitines, CoQ-10 and D-ribose should be considered by every reputable cardiologist who wishes to improve his or her patients' quality of life and survival rate. My message has been to reduce human suffering using whatever vitamins, mineral and nutraceuticals, in addition to the latest medicines and techniques. Now my mission is to teach cardiologists across the country about ATP and the heart. **WF**

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