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On The COVER

Enhancing Cardiac Energy with Ribose

By Stephen T. Sinatra, MD, and James C. Roberts, MD

After years of performing angiograms and emergency cardiac procedures, two cardiologists—Drs. Stephen Sinatra and James Roberts—grew weary of seeing their patients fail to achieve lasting cardiovascular health. As they began to integrate complementary therapies such as coenzyme Q10, L-carnitine, and D-ribose into their patient care protocols, they noticed an astonishing result: hospital admissions for their heart patients dropped dramatically.

In the following excerpt from their new book Reverse Heart Disease Now, these forward-thinking physicians report how they use D-ribose in their practice to help patients suffering from coronary artery disease, congestive heart failure, peripheral arterial disease, and more. Their impressive results may well herald a new era of preventive cardiology that uses integrative approaches to prevent and reverse cardiovascular disease, before catastrophe strikes.

D-ribose is the new kid on the heart supplement block. As a building block of ATP (adenosine triphosphate), it rapidly restores depleted energy in sick hearts.

You probably haven't heard about D-ribose. But you will. It's that good. Every cell in the human body makes some of this simple sugar molecule, but only slowly and to varying degrees, depending on the tissue. The liver, adrenal glands, and fat tissue produce the most—enough to serve their purpose of making compounds involved in the production of hormones and fatty acids. But tissue elsewhere has little.

Red meat, particularly veal, contains the highest dietary concentration of D-ribose, but not significant enough to provide any meaningful nutritional support, especially to unwell individuals. Heart, skeletal muscle, brain, and nerve tissue can only make enough D-ribose to manage their day-to-day needs when their cells are not stressed. Unfortunately, these cells lack the metabolic machinery to make D-ribose quickly when they come under metabolic stress such as blood and oxygen deprivation (ischemia). When oxygen or blood flow deficits are chronic, as in heart disease, tissues can never make enough D-ribose. Cellular energy levels become depleted.

THE DOCTOR AS GUINEA PIG

When Dr. Roberts heard about D-ribose, a light bulb immediately went on in his head. For some time, he had been using L-carnitine and CoQ10 in his medical practice to boost energy metabolism in sick hearts, but neither L-carnitine nor CoQ10 can rebuild the metabolic energy pool once it has been depleted by heart disease. He wondered if D-ribose could be the missing link.

Before trying it on patients, he decided to try it first on himself. As a marathon runner, he knows the importance of energy recovery. It is the impaired recovery of the muscle ATP pool that causes the pain, soreness, stiffness, and fatigue that follow long-distance training runs. He found that taking D-ribose before and after a run eliminated these problems. The usual muscle pain and soreness that persist for a day or two, or even three, were gone. He was no longer fatigued in the days after a hard workout. He was convinced!

In his cardiology practice, he offers patients an enhanced external counterpulsation (EECP) program, a noninvasive method that restores the flow of oxygenated blood in patients with recurrent or inoperable coronary artery disease. Before D-ribose, most of the patients on EECP experienced good improvement. After adding D-ribose, improvement made a quantum leap to great. In hardcore cases like these, supplying oxygen alone to the chronically flow-deprived heart cells was not enough. Yes, the cells were deficient in CoQ10 and L-carnitine, but above all they lacked the precursors of ATP.

He began to put patients with angina and heart failure on D-ribose. They also improved. Time after time, Dr. Roberts found remarkable improvement in cardiac function measurements, exercise tolerance, quality of life, and recovery from fatigue. He was

hooked and soon was lecturing about D-ribose at medical meetings.

THE ABCS OF D-RIBOSE

Ischemia may cause the heart to lose up to 50% of its ATP pool. Even if blood flow and oxygen are restored to normal levels, it may take up to 10 days for an otherwise healthy animal heart to rebuild cellular energy and normalize diastolic cardiac function. In studies, when oxygen-starved animals receive D-ribose, energy recovery and diastolic function return to normal in an average of two days. When patients with CAD (coronary artery disease) are treated with D-ribose, symptoms and treadmill time improve significantly within one week.

Several factors determine who should take D-ribose supplements and when they should be taken. Age is one consideration. We believe 20-25% of people over 45, men and women alike, show early signs of diastolic cardiac dysfunction (stiff heart) and are at risk of contracting heart failure later in life. This is especially true in people with high blood pressure, people taking statin drugs, and in women with severe mitral valve prolapse. For these people, D-ribose supplementation increases the cardiac energy reserve and helps the heart restore normal diastolic cardiac function.

We also know that the health of our mitochondria suffers as we age. As a result, even minor metabolic stress can have a dramatic effect on cellular energy stores in an aging population.

Patients with heart disease on drugs intended to increase the contractile strength of their heart are also good candidates for D-ribose. These drugs, known as inotropic agents, make the heart beat harder. This places considerable strain on the heart's ability to supply enough energy to support the extra metabolic stress. Long-term treatment with these agents drains the energy reserve, essentially running the heart out of energy. Patients with heart failure, chronic coronary artery disease, or cardiomyopathy should take D-ribose to offset the energy-draining effects of inotropic drugs such as digoxin. Research shows that supplementation reduces the energy drain without any negative impact on the activity of the drug.

Patients with coronary artery disease and persistent symptoms remain in a chronic state of energy depletion, constantly fatigued, weak, and with their heart function progressively worsening. These patients will almost certainly advance into congestive heart failure without improvement of the energy state of their heart. Restoration of their energy pool can only be accomplished through the pathway of energy metabolism regulated by the availability of D-ribose.

We cannot overstate the effect of D-ribose supplementation on maintaining energy levels. Any tissue that relies heavily on aerobic energy metabolism, such as the heart and muscles, will be severely affected by any amount of oxygen deprivation. The problem is ATP drain. The solution is to give it back!

Fibromyalgia patients are chronically fatigued and subject to muscle pain, soreness, and stiffness that can be associated with depleted cellular energy reserves. We are learning that patients with fibromyalgia and chronic fatigue syndrome have faulty ATP metabolism, so it makes perfect sense to use D-ribose to help them.

Unlike many other nutrients, we can't really talk about a formal D-ribose deficiency in tissue. Deficiencies refer to tissue concentrations of nutrients that fall to below-normal levels. D-ribose is not stored in cells in its free form; thus, there is no "normal" level of D-ribose in tissue. Instead, cells are faced with the task of making D-ribose in response to a specific metabolic demand. And this is where they get into trouble, because making D-ribose is a slow and time-consuming process in virtually all cells.

"YOU FIXED LOUIS"

Louis came to Dr. Sinatra's office suffering from severe coronary artery disease. Although previously treated with a stent placed in his left anterior descending artery, he still had severe blockage in an important arterial branch called the diagonal. The branch would have been difficult to dilate with a stent and unreasonable to bypass with surgery.

Louis had stubborn angina because of this unresolved situation. He experienced chest pain with normal activity, such as walking across a room, or from just mild emotional stress. He had visited several cardiologists for his heart problem. They gave him a number of standard heart drugs, but his situation persisted, and he decided to see Dr. Sinatra for a fresh opinion.

Testing showed that Louis had high levels of uric acid in his blood, indicating faulty ATP metabolism. He had already been taking low doses of L-carnitine and CoQ10. He needed higher doses, and he needed D-ribose to build his ATP pool. In just a few days, Louis showed such remarkable improvement that his son-in-law called and reported, "You fixed Louis!"

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THE RISE OF D-RIBOSE

Until 1944, D-ribose was thought to be primarily a structural component of DNA and RNA with little physiological significance. But a series of studies, culminating in 1957, revealed that this sugar molecule played an intermediate role in an important metabolic reaction called the pentose phosphate pathway. This reaction is central to energy synthesis, the production of genetic material, and for providing substances used by certain tissues to make fatty acids and hormones.

The D-ribose connection to cardiac function was made by the physiologist Heinz-Gerd Zimmer at the University of Munich. In 1973, he reported that energy-starved hearts could recover faster if D-ribose was given prior to, or immediately following, ischemia (oxygen deprivation). Five years later, he reported the same effect in skeletal muscle and also showed for the first time that the energy-draining effects of drugs that make the heart beat more strongly (inotropic agents) could be lessened if D-ribose was given along with the drug. Zimmer and his research colleagues later proved that D-ribose was the limiting element in energy recovery in ischemic tissue and that energy synthesis could not occur without it.

Zimmer's research sparked a flurry of research on humans, rats, rabbits, guinea pigs, dogs, and even turkeys, all with similar results. D-ribose administration significantly improved energy recovery in ischemic, hypoxic, or cardiomyopathic hearts and skeletal muscle, and it improved functional performance of the tissue. In addition, studies with several common heart drugs—those used even today—showed that D-ribose administration did not negatively affect (and in many cases helped) the action of the drug on the heart.

The most significant findings of the studies underscored the dramatic effect that D-ribose administration played in both energy restoration and the return of normal diastolic cardiac function. A clinical study from Zimmer's group in Munich in 1992 showed that D-ribose administration to patients with severe, stable coronary artery disease increased exercise tolerance and delayed the onset of moderate angina. Since this groundbreaking study in coronary artery disease, the benefits of D-ribose have been reported for cardiac surgery recovery, heart failure and neuromuscular disease treatment, restoration of energy to stressed skeletal muscle, and control of free-radical formation in oxygen-deprived tissue.

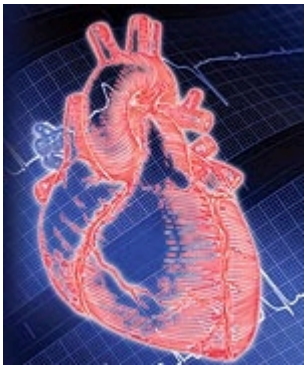
Several notable papers were published in 2003. One study showed that D-ribose improved diastolic functional performance of the heart, increased exercise tolerance, and significantly improved the quality of life of patients. Researchers have even extended their sights to healthy hearts and bodies and documented benefit from D-ribose supplements to improve athletic performance.

Research continues here and abroad. Yet, despite the powerful scientific evidence, very few US physicians have even heard of D-ribose outside of their first-year medical school biochemistry class, and fewer still recommend it to patients. We lucky ones who are familiar with it have the wonderful gratification of seeing it help our patients on a regular basis.

OUR RECOMMENDATIONS

Supplemental D-ribose absorbs easily and quickly through the gut and into the bloodstream. About 97% gets through.

How much D-ribose do you need? That question can only be answered with another question, "What do you want it to do for you?



Studies have shown that any amount of D-ribose you give to energy-starved cells gives them an energy boost. At the University of Missouri, researcher Ronald Terjung has shown that even very small doses (the equivalent of about 500 mg) of D-ribose increase energy salvage in muscles by more than 100%. Larger doses increase the production of energy compounds by 340-430%, depending on the type of muscle tested, and improve the salvage of energy compounds by up to 650%. Most amazing is that when muscles are supplemented with D-ribose, they continue to add to their energy stores even while they actively work! Until this study was reported, it was thought that muscle energy stores were only refilled in muscles at rest.

An adequate dose of D-ribose usually results in symptom improvement very quickly—sometimes within a few days. If the initial response is poor, the dose should be increased until the patient feels relief. Logically, the sickest patients stand to gain the most.

Patients with arterial and heart disease who chronically choke off oxygen delivery to their tissues need to take a higher dosage simply to allow enough of it to work its way through the clogged vessels into the energy-parched portions of the heart. We start those patients at higher dosages and monitor their progress. With progress, the dosage can be reduced to the lowest possible point at which good energy and quality of life are maintained.

Those patients must take D-ribose every day. Missing even one or two days will negatively impact cellular energy, which will show up as weakness and fatigue.

We don't know the optimal level for every patient or every pathological condition, but we can make some recommendations as dosage starting points:

- 5 grams (if using a powder, two teaspoons) daily for cardiovascular prevention, for athletes on maintenance, and for healthy people doing strenuous activity
- 10-15 grams daily for most patients with heart failure, other forms of ischemic cardiovascular disease, or peripheral vascular disease, for individuals recovering from heart surgery or heart attack, for treatment of stable angina, and for athletes working out in chronic bouts of high-intensity exercise
- 15-30 grams daily for patients with advanced heart failure, dilated cardiomyopathy, or frequent angina, for individuals awaiting heart transplant, and for people with fibromyalgia or neuromuscular disease.

Start at the upper level of each range for patients with heart or peripheral vascular disease. We recommend that daily doses up to 10 grams be taken as two 5-gram doses with morning and evening meals or just before and just after exercise or activity. Larger doses (15 grams per day or more) should be taken in three or sometimes even four smaller doses of about 5 grams each. Daily doses in excess of 30 grams are seldom needed. Most heart patients will stabilize at about 10 grams per day.

Once a patient responds with a reduction in symptoms, the dosage may be gradually reduced until a maintenance level is reached. Sometimes patients well maintained at a certain dose may require an increase due to changes in their activity level or changes in their cardiac drug therapy, such as the addition or deletion of beta blockers or calcium channel blockers. It cannot be overemphasized that patients must continue on D-ribose therapy, or relapses will almost certainly occur. D-ribose is quickly absorbed and leaves the blood rapidly. Therefore, assessing blood levels of D-ribose is not helpful, in addition to being very costly.

PRECAUTIONS

The toxicology and safety of D-ribose have been exhaustively studied. The supplement is 100% safe when taken as directed. Thousands of patients have taken D-ribose at dosages up to 60 grams per day with minimal side effects. However, even though there are no known contraindications of D-ribose therapy, we recommend that pregnant women, nursing mothers, and very young children refrain from taking D-ribose simply because there is not enough research on its use in these populations.

D-ribose can actually lower blood glucose levels; therefore, insulin-dependent diabetics should check with their physicians before starting on the supplement.

Reported side effects are minimal and infrequent. Patients may experience light-headedness if they take a large dosage (10 grams or more) on a completely empty stomach. Take D-ribose with meals, or at least mixed into juice, milk, or fruit, to offset the blood-glucose-lowering effect.

There are no known adverse drug or nutritional interactions associated with D-ribose use.

Excerpted from Reverse Heart Disease Now by Stephen T. Sinatra, MD, and James C. Roberts, MD (John Wiley & Sons, Inc., Hoboken, New Jersey, 2007).