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**REPORT**

# **D-Ribose: ENERGIZE YOUR HEART, SAVE YOUR LIFE**

## **Rejuvenate Cardiac Cellular Energy Production**

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After a heart attack, there is a limited window of time to restore cellular energy production. Failure to rejuvenate blood-deprived cardiac cells results in catastrophic heart muscle damage.

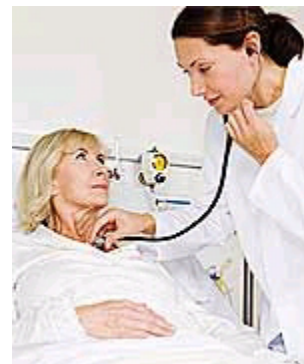
New studies reveal how a low-cost nutrient can protect against cell damage that occurs during a heart attack and help rejuvenate heart muscles that have suffered injuries from previous ischemic (no blood flow) events.<sup>1</sup>

### **SUPPORTING “CARDIAC REJUVENATION”**

Cardiologists are slowly recognizing specific nutrients play a vital role in preventing and treating heart disease—particularly ischemic heart disease (caused by coronary artery occlusion) that underlies most heart attacks. When deprived of blood flow, the injured heart muscle becomes flabby and unable to pump blood efficiently.



The sharp drop in ATP (adenosine triphosphate) levels experienced by heart muscle cells during the obstruction of blood flow, and the long delay in restoring those levels to normal even after blood flow returns is critically important after a heart attack. This so-called ischemia-reperfusion injury is now known to be the major culprit that produces long-term heart damage in survivors of heart attacks, rendering tissue inordinately vulnerable to free-radical damage produced by the oxygen-rich (yet life-saving) re-flow of blood into the injured area.<sup>2-4</sup> In fact, one researcher this year referred to the heart mitochondria (the site of all that ATP production) as “the gates of life and death!”<sup>5</sup> Clearly, helping heart muscle cells to recover rapidly from a cardiac event is a major priority in preventing long-term damage.



A natural ingredient for building new ATP, D-ribose is an important component of a “cardiac rejuvenation” regimen. Animal studies show that it dramatically increases ATP levels in the critical reperfusion period after a heart attack (the time when blood flow is restored and cells use energy at extremely high levels to repair the damage). This provides much-needed energy levels to block further injury and start the healing process.<sup>6-8</sup>

A landmark interventional study demonstrated these effects dramatically.<sup>9</sup> The cardiac arrest induced during certain kinds of heart surgery (such as bypass surgery) causes heart muscle function to deteriorate quickly, even in relatively healthy areas of the heart, an effect that is associated with low ATP levels, which can severely delay recovery following surgery. As a result, the scientists administered D-ribose to the heart during surgery, reasoning that they could “stoke up” heart muscle in advance with the necessary ingredients for ATP. This procedure produced dramatic results in the experimental study consisting of a full hour of cardiac arrest. The ribose-supplemented experimental group showed significant improvement in heart muscle function compared with controls—and the amount of improvement correlated directly with the quantity of ATP in the heart muscle!<sup>9</sup>

Since then, convincing evidence has continued to accumulate that D-ribose directly contributes to the rejuvenation of injured heart muscle.<sup>10-13</sup>

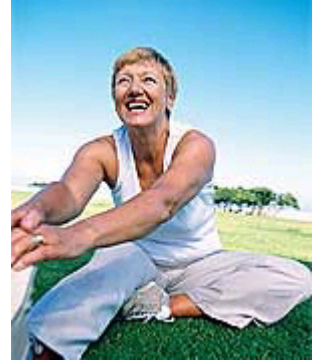
In essence, these studies established the powerful protective effect of D-ribose and other ATP components under the most stressful situation heart muscle can encounter—complete cessation of blood flow followed by sudden return of oxygen-carrying blood.

## REJUVENATING HUMAN HEARTS

Some exciting studies have emerged showing how D-ribose affects active human heart tissue and its function.<sup>14,15</sup> Investigators have shown how increased ATP levels translate into improved heart muscle function, better blood flow, and quicker recovery with protection from the ravages of reperfusion-induced oxidation.

Ischemic (no blood flow) events such as a heart attack cause areas of the heart muscle to “hibernate” exactly as if they were awaiting a higher-energy environment to return to their normal rates of activity. Cardiologists at the Oregon Health Sciences

University studied this phenomenon in a group of patients with coronary artery disease, subjecting them to a “thallium stress test.”<sup>16</sup> In this test, patients are injected with a radioactive tracer immediately following moderate exercise, and the distribution of the tracer is followed using special cameras. The patients received either D-ribose infusion or a placebo and the tests were repeated at four and 24 hours, respectively. The groups were then switched to receive the opposite preparation. The results were stunning—the images taken just four hours after D-ribose infusion revealed 21 areas of defective tissue that had not been seen in the placebo group, indicating that D-ribose was “waking up” viable areas of heart muscle and helping improve identification of viable ischemic heart muscle.<sup>16</sup> A larger study published the same year showed similar results.<sup>17</sup> These studies show that D-ribose not only enhances cardiologists’ ability to accurately gauge the degree of heart damage, but also suggest strongly that this supplement might hasten the recovery of healthy heart function following a heart attack.



## CARDIOPROTECTION

Survivors of heart attacks face the prospects of permanently damaged heart muscle, which saps the heart’s pumping abilities and produces a host of symptoms from mild exercise intolerance to severe congestive heart failure. And since rehabilitation for practically any heart condition requires regular moderate exercise, it is vital to assure that heart muscle cells optimize ATP levels.

A problem aging humans face is that their heart muscle enlarges and becomes “stiff.” The result of this enlargement is a reduction in ability to contract to pump blood out and to relax to allow blood in. People with ventricular hypertrophy often have limited exercise tolerance and their hearts are often especially vulnerable to ischemia and subsequent further damage.

In a study with far-reaching implications for humans, researchers examined the effects of D-ribose in animals to determine whether the supplement, given in advance, could protect their hearts against experimentally induced ischemia.<sup>18</sup> They also studied the effects of D-ribose in animals with hypertension and enlarged heart muscles, the same hypertrophy that so commonly develops in humans with sustained high blood pressure.

The first study results were stunning. The heart muscles of healthy animals given D-ribose before ischemia held out 25% longer before the onset of irreversible injury and had significantly elevated stores of energy-rich glycogen. In human terms, that could translate into valuable extra time for modern emergency medical services to do their part, and could result in dramatically improved survival after stabilization. These researchers also showed that in the hypertensive rats with ventricular hypertrophy, D-ribose treatment significantly improved ventricular function by as much as 25%, increasing the hearts’ ability to “squeeze” at the appropriate times and pumping blood more effectively. The translation for humans? Similar results would allow those with ailing hearts to deliver more blood to vital energy-hungry body organs and structures—including the skeletal muscles that so readily fatigue and limit exercise tolerance.



## WHAT YOU NEED TO KNOW: D-RIBOSE

- Fatigue and exhaustion often occur as a result of depletion of the vital molecule called ATP in human muscle.
- Injured or heavily used muscle is particularly vulnerable to low ATP supply and is slow to recover those levels.
- A simple sugar molecule, D-ribose, is one of the key components of ATP. The more D-ribose that is available, the faster ATP levels return to normal.
- D-ribose supplementation has been shown to boost heart muscle function following heart attacks, and to improve blood pumping in people with congestive heart failure.
- Better heart muscle function after D-ribose supplementation can lead to better delivery of energy-rich blood to skeletal muscles, revving them up for increased activity.
- Increased ATP levels in skeletal muscle following D-ribose supplementation can help to reduce the muscle pain and fatigue that prevent people from keeping up their vital exercise regimens.
- Cardiologists and exercise physiologists are increasingly turning to D-ribose as a means of “rejuvenating” their patients’ cardiac and skeletal muscles and improving their quality of life.

### PROTECTING PATIENTS WITH HEART DISEASE

The results of these studies also have strong implications for the benefits of D-ribose in protecting people with congestive heart failure, who just don’t have the cardiac power to pump blood vigorously from their hearts and around the body. The result is often lack of energy, poor exercise tolerance and, in more severe cases, liver and lung complications, which can ultimately be fatal. Restoring the heart muscle’s “tone” in patients with congestive heart failure is the goal of a host of drug treatments including diuretics, digoxin, and others. In 2003, German researchers, however, took a more natural approach—they provided daily oral D-ribose supplements or placebo for three weeks to 15 people with congestive heart failure.<sup>19</sup> The groups then reversed their treatment assignments.

During the period of D-ribose supplementation, the patients showed dramatic improvements in their hearts’ ability to fill and empty efficiently—changes critical to reducing fluid accumulation throughout the body, and to boosting energy levels as tissues gain oxygen and nutrients from the restored blood flow. Perhaps most importantly from the patients’ own standpoint, they reported substantial improvements in quality of life while on the active supplement. This general sense of improved energy and well-being is vital to reinvigorating people and getting them started on making the lifestyle changes (such as increased exercise) that we know are so important to maintaining cardiovascular health.

This study followed an earlier publication of a seminal paper by German cardiologists who studied the effect of D-ribose in 20 men with severe coronary artery disease that was sharply limiting their exercise tolerance (the ability to engage in mild physical activity without either painful symptoms or ominous changes in electrocardiogram [EKG] tracings).<sup>20</sup>

The researchers tested the men with two treadmill exercise tolerance tests to determine their baseline level of physical function. Subjects were then randomly assigned to receive either D-ribose 60 grams/ day by mouth or a placebo for three days. Next, the exercise tolerance tests were repeated, with the subjects walking until EKG changes mandated a halt. Men who had taken the supplement were able to increase their treadmill walking time to 4.6 minutes, compared with just 3.7 minutes in the control group—a 24% improvement. The ribose-supplemented men also showed a significant improvement in the time it took to develop moderate angina (chest pain) compared with their baseline times—a change that the control group did not experience. This study provided another way to promote heart function in people with significant cardiac disease. Of course had these same patients been given ubiquinol CoQ10, acetyl-L-carnitine, taurine, and other cardiac-energizing nutrients, even greater improvements may have been observed, or a lower dose of D-ribose needed.

### ENERGIZING SKELETAL MUSCLE

“Cardiac rejuvenation” is clearly one of the important ways in which D-ribose can produce benefits for people with heart problems. But what about the all-important skeletal muscles that are called on to actually use the energy supplied by that increased blood flow and improved sense of well-being? There’s good news on that front as well, as a series of remarkable studies has shown.

A regular exercise program is critical to prevention of cardiovascular disease, as well as to the all-important rehabilitation following a heart attack, stroke, or other potentially catastrophic event.<sup>21,22</sup> Yet fewer than 50% of patients at risk actually participate in regular, structured exercise programs aimed at improving or maintaining cardiovascular health.<sup>23</sup> Many people simply have trouble mustering the energy they need to start and maintain even a modest program of physical activity. One study found that exercise-induced physical fatigue was the most important reason people stopped their workouts.<sup>24</sup> That's understandable—vigorous exercise can drop muscle ATP levels by up to 20%, with up to a 72-hour recovery period being required when muscles have been worked hard.<sup>25,26</sup>

The “wiped-out” feeling many of us experience after exercise is also caused by the leakage of ATP breakdown products from muscles into the bloodstream.<sup>27</sup> And though personal trainers love to chant “no pain, no gain,” the truth is that too much pain can lead to no gain at all! Once again, D-ribose is vital to keeping our muscles' ATP-based energy stores at peak capacity.<sup>28,29</sup> And that can mean less “afterburn” and more enthusiasm for the next workout.

There's excellent science to back up the idea that D-ribose is good for working muscles. Exercise physiologists showed that supplementing the muscles with D-ribose increased the total amount of ATP produced by up to four-fold, providing a substantial “bank” of energy that could be called on for use when needed.<sup>30</sup> And when physiologists in Missouri provided D-ribose to working muscles, they demonstrated as much as a six-fold rise in the rate at which ATP components were recycled for use (recycling ATP is much faster and more efficient than building it from scratch).<sup>29,31</sup>

Danish sports and exercise physiologists showed that human muscle lost ATP after extreme exercise just like in experimental models and they also noted that the exhausted muscles took longer to replenish their ATP levels than rested muscles.<sup>27</sup> That led them to speculate that supplementing human sprinters with D-ribose might speed the recovery of their muscles' ATP levels.

In 2004, they published a landmark paper showing that, in fact, three-times daily supplements of D-ribose for three days following extreme sprint training caused ATP levels to return to normal within 72 hours, while in placebo recipients ATP levels remained depressed.<sup>32</sup> It is important to note here that in this study as well as in many others, the D-ribose supplements did not increase muscle strength or power.<sup>33-37</sup> So don't think of D-ribose as a “strength-training” supplement. The restoration of normal ATP levels in “worked-out” muscles is probably what reduces the “wiped-out,” “spongy,” or “burning” feelings that people often experience following a workout.

## D-RIBOSE—FUEL FOR HEART AND MUSCLE FUNCTION

D-ribose is a simple sugar molecule with a wealth of functions in human and animal biology. Perhaps its most fundamental role is as a component of ATP, the universal energy carrier in the body's cells.<sup>32</sup> ATP molecules store energy as they are built up and release it as they are broken down—the more energy a cell requires, the more ATP it consumes. In fact, humans “burn” an amount of ATP equivalent to their own body weight every day!<sup>40</sup>

Every single process undergone by living cells requires energy—even at rest, we are continually breaking down ATP molecules. And that means that we have a constant need for the components of ATP molecules, including D-ribose. Cells can make new supplies of D-ribose, but the process is considerably slower than the breakdown of ATP<sup>28,31</sup>—this can leave a substantial “deficit” in the amount of energy a cell can utilize.<sup>29,31</sup> In fact, it has been shown that even an overnight rest period is not long enough for a person to recover their normal ATP levels after a bout of strenuous exercise.<sup>25,26,29</sup> It's no wonder that many of us feel “drained” after a hard workout—we are in fact drained of the very substances we need to make use of all of our available energy!

When cells don't have enough D-ribose to restore ATP levels quickly back to normal, they turn to alternate energy-generating processes. These are less efficient and produce much higher levels of damaging waste products that cause muscle burning and cramping and that can also inflict long-term damage through the oxidant stress they induce in muscle and heart tissues, leading to further dysfunction, injury, and pain.<sup>10,29,41,42</sup>

Fortunately, research is demonstrating that ATP levels can be speedily brought back to normal if sufficient D-ribose is available. This has been demonstrated in the case of ATP depletion following strenuous exercise,<sup>28,29,32</sup> which has implications for those who want to maintain health through lifestyle modifications. Perhaps more dramatically, D-ribose also restores ATP to normal or near-normal levels after the heart muscle injury seen in a heart attack.<sup>6,7,11,14,19,20,31,43-47</sup>

D-ribose is not a vitamin—cells can and do manufacture it themselves, given enough time and raw materials. But when stressed by injury or high energy demands, they can't keep up—leading one nutritional biologist to include D-ribose in a list of “conditionally essential” nutrients—those that have to come from outside the body under conditions, such as heart disease, which impose exceptional stresses on human tissue.<sup>48</sup>

## WORD OF CAUTION

Numerous human studies have shown that intravenous infusion or high-dose oral supplementation with D-ribose produces hypoglycemic (blood sugar-lowering) effects.<sup>32,38,39</sup> This effect seems to be dose-related, with larger doses producing greater declines in blood glucose. Taking D-ribose with meals may help offset its hypoglycemic effect.

## SUMMARY

For millennia, people have believed that as we age, we naturally lose energy and vitality, but increasingly we're learning that those losses are not inevitable. Humans, like all living things, must maintain high levels of ATP to support physical activity, and damaged or stressed muscle is slower at restoring those critical levels back to normal. And when ATP levels drop and cannot be restored quickly, we do indeed feel "drained" of energy.

But remarkable scientific progress has been made in the past few decades. Scientists are discovering that simply by providing injured, ailing, or fatigued muscle tissue with the ingredients for ATP, that tissue can be "rejuvenated," restoring energy levels and boosting function. D-ribose, a natural sugar molecule with no known side effects, is one of those key ingredients. D-ribose supplementation powers damaged heart muscle back to near-normal levels of function, allowing victims of cardiovascular disease to begin the vital rehabilitation process. D-ribose can also help restore ATP levels in skeletal muscle, relieving pain and weakness post-exercise, and helping people to actually maintain the moderate level of increased exercise that is so critical to preventing heart disease and to recovering from it if it does occur. D-ribose can improve both cardiac energy and quality of life—a winning combination!

If you have any questions on the scientific content of this article, please call a Life Extension Health Advisor at 1-800-226-2370.

## WHAT IS THE RIGHT DOSE OF D-RIBOSE?

Unlike many other nutrients that operate at the milligram (or even microgram) level, D-ribose is such an important constituent that the body utilizes it in quantities measured in grams. The optimum amount of D-ribose will vary with each individual and with each condition being prevented or treated.

For healthy people using D-ribose as part of an exercise program, scientists have studied D-ribose in doses as low as 625 milligrams/day<sup>37</sup> (not surprisingly, this dose was ineffective) to as high as 16 grams/day.<sup>36</sup>

In management of injured heart muscle, experimental studies showed good effects with doses equivalent to about 14 grams/day for a 60-kilogram (132-pound) man for right ventricular hypertrophy,<sup>49</sup> while the most dramatic human trial on exercise tolerance in people with coronary artery disease used fully 60 grams/day as four divided doses of 15 g each.<sup>20</sup> Finally, a recent study of people with fibromyalgia and chronic fatigue syndrome showed clinically significant improvements in fatigue and pain with 5-gram doses given three times daily (15 g/day total).<sup>50</sup>

Cardiologists with extensive experience using D-ribose in their patients<sup>1</sup> recommend the following dosing regimen based on the needs of the person taking the supplement:

| PATIENT GROUP   | STARTING DOSE    |
|---|------------------|
| Basically healthy individuals who want cardiovascular protection and greater comfort following strenuous activity                   | 5 gram/day       |
| Athletes working out in chronic bouts of high-intensity exercise  | 10-15 gram/day   |
| Patients with mild-to-moderate heart failure, other forms of ischemic cardiovascular disease, or peripheral vascular disease        | 10-15 gram/day * |
| Individuals recovering from heart surgery or heart attack, for treatment of stable angina   | 10-15 gram/day * |
| Patients with advanced heart failure, dilated cardiomyopathy, individuals awaiting heart transplant, or people with frequent angina | 15-30 gram/day * |
| People with fibromyalgia or neuromuscular disease   | 15-30 gram/day   |

\* These cardiologists<sup>1</sup> recommend starting at the upper level of these ranges for these cardiovascular conditions, dividing total daily dose into multiple 5-g individual doses. As patients notice reductions in symptoms, they may choose to gradually reduce the doses until a comfortable maintenance level is reached. Naturally, individuals may want to increase their doses shortly before increased activity.

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