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What You Need to Know About Your Mitochondria

Analysis by Dr. Joseph Mercola ✔ Fact Checked | March 18, 2022

STORY AT-A-GLANCE

- In simple terms, mitochondria are the powerhouse of your cells, producing about 90% of the energy being generated in your body
- Everything that happens in your body, each and every muscle contraction and relaxation, biochemical cascade, cellular regeneration, detoxification and so on requires energy
- Free radicals formed at the level of the mitochondria are typically extremely harmful, which is why you need to minimize them. Two of the most effective ways to do this are exercise and calorie restriction (fasting)
- Mitochondria also act as the coordinator for apoptosis, or programmed cell death — an important process that ensures the death of malfunctioning cells that might otherwise turn into cancer
- If your genetic heritage stems from equatorial regions, you will tend to have less brown (heat-generating) fat, and hence less mitochondrial uncoupling, which raises your risk of chronic disease. To counteract this, you will need to exercise regularly and regularly engage in cold thermogenesis training

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When it comes to health and disease prevention, your mitochondrial health and function simply cannot be overstated. If your mitochondria are not functioning well, nothing else will either. Optimization of mitochondria is also a central key for life extension. Dr. Lee

Know, who is a naturopathic physician, has written a must-read book on this topic called "**Mitochondria and the Future of Medicine: The Key to Understanding Disease, Chronic Illness, Aging, and Life Itself**."

Know has been a passionate student of mitochondria for quite some time. "I've always been interested in antiaging and longevity, but that was not the motivation behind the book," he says. That motivation grew out of an interest in Coenzyme Q10. Animal research was showing that age-related female infertility was closely linked to mitochondrial dysfunction and aging mitochondria, and could be reversed through CoQ10 supplementation.

Fertility clinics in Canada started to use CoQ10, and through his work as a consultant for a supplement company working with a particularly bioavailable form of CoQ10, Know was invited as a spokesperson for the brand. He gave presentations to doctors and nurses, explaining how the supplement could benefit their patients.

> *"As I started to do the research, I started to understand the connection of healthy mitochondria to not just age-related female infertility but to pretty much all degenerative diseases, including the aging process,"* he says.

> *"One of the things I came to realize is that there is a lot of good information out there, a lot of good primary research that's been done, but I didn't really see any one resource that summarized everything. That's what I wanted to do — pull all these different resources together to give a starting point for anyone that is really interested in the mitochondria and understanding [their] importance."*

Mitochondria 101

So, what exactly are mitochondria, and why are they so crucial for good health? In the simplest terms, mitochondria are the powerhouse of your cells, producing about 90% of the energy being generated in your body. What many fail to realize is that absolutely everything that happens in your body, each and every muscle contraction, biochemical

cascade, cellular regeneration, detoxification and so on requires energy. Nothing can occur in an energy vacuum.

> *"A lot of things happen in the cell that people don't even think [about], like the transfer of ions across membranes, or the maintenance of the shape of the cytoskeleton. For the microtubules to maintain their shape, they require an input of energy.*
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> *Literally everything that happens in the cell requires energy, and because the mitochondria is so critical to that energy supply … any time you have a decrease in that energy production, things can start to fall apart."*

Mitochondria also have other radically important functions. For example, they act as the coordinator for apoptosis, or programmed cell death — an important process that ensures the death of malfunctioning cells that might turn into tumors lest they be cleaned out. Know explains:

> *"Apoptosis is basically cell suicide. Over the course of a cell's life … it's going to [be] damaged. When that damage crosses a threshold, signals are sent to the cell that tell it, 'You're no longer functional, you better commit suicide for the greater good of the organism.' What's interesting is that the newest research has shown that it's the mitochondria that … initiate that cell suicide program …*
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> *It's the mitochondria that receive all those signals [and] determine whether or not that threshold has been reached … It's also interesting to note that if your mitochondria are dysfunctional, first of all it might not be able to understand those signals properly and not give the signal for apoptosis when it's supposed to happen.*
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> *The other thing is that all those different things that happen in the apoptosis cascade also require an input of energy. So, even though it might be able to read the signals properly and give the signal that it's time to commit suicide, if there's not enough energy being produced … defective cells will survive and*

multiply … [So] dysfunctional mitochondria are the basis behind what we know as cancer."

Energy Production Basics

As mentioned, about 90% of the energy produced within your cells occurs in your mitochondria, with a small portion of that occurring outside the mitochondria. The energy process starts in the cytosol (the fluid compartment of the cell), in a process called glycolysis.

Once that process is done, the end products of glycolysis then enter the mitochondria and participate in the next phase of energy production, which is called the tricarboxylic acid (TCA) cycle, better known as the Krebs cycle.

Out of that Krebs cycle comes other energy molecules that then get fed into the last part of the energy production process — the electron transport chain. This is where things can start going wrong, leading to dysfunctional mitochondria. Consumed calories are converted into electrons that then enter complex I or complex II of the electron transport chain. Those two complexes then pass on electrons to CoQ10, and then down the chain until it reaches complex IV.

"Now, complex IV is a very unique part in the cell because it's the only place in the cell where we can take those electrons and enzymatically react them with oxygen to create water," Know explains. *"The problem is, if those electrons don't reach complex IV and spill out of the electron transport chain prior to complex IV, it can prematurely react with oxygen, creating a free radical called superoxide.*

That is where the damage can start to occur because those superoxide radicals generated at the level of the electron transport chain are created in the immediate proximity of mitochondrial DNA [which] is particularly susceptible to damage. So, any time those free radicals are generated, you can have damage

to the DNA in the mitochondria. If those DNA are damaged, you can't produce the proteins it codes for and everything starts to fall apart."

Nuclear Versus Mitochondrial Repair Mechanisms

It is important to understand that free radicals are not universally toxic. You need some, and they serve useful and beneficial roles with important signaling functions. That said, most of the superoxide radicals formed at the level of the mitochondria are harmful, which is why you need to minimize them.

Cellular damage is essentially occurring around the clock, and your body has built-in repair mechanisms to continually address this damage. As mentioned, compared to the DNA in your cell's nucleus, the DNA in your mitochondria are far more susceptible to damage.

Nuclear DNA are protected by elaborate proteins called histones, which form a shield around the DNA. Mitochondrial DNA does not have these protective proteins. Nuclear DNA also have massive reams of DNA that do not necessarily code for protein, commonly referred to as junk DNA (although we're now starting to realize they too perform important functions; we just have not identified them yet). In the mitochondria, on the other hand, DNA is tightly packed and there's no junk DNA.

Lastly, the DNA in your cell's nucleus have elaborate and highly efficient repair mechanisms, whereas mitochondrial DNA do not have very good repair mechanisms. So, to protect your mitochondrial DNA, it's important to minimize the generation of free radicals in the electron transport chain.

As explained by Know, "Any time we have damage or free radicals being generated that exceed the capacity of the repair mechanisms, you're going to cause irreversible damage. That's what the whole point is — to stop [the damage]."

Efficient Fat Burning Minimizes Mitochondrial Damage

Indeed, that's the premise of my book "**Fat for Fuel**," which details strategies aimed at minimizing the production of excess free radicals while allowing biologically important free radicals to be maintained. What we're now finding is that it's the divergence from our ancestral diet — the massive prevalence of processed, unnatural foods and excessive amounts of added sugars, net carbs and industrial fats — that causes a majority of the damage.

High-carb, processed food diets prevent your body from efficiently burning fat as its primary fuel, and burning fats and ketones is far more efficient, inducing far less oxidative stress, than burning carbs. So, a foundational dietary strategy to optimize your mitochondrial health is to eat the right fuel. Once you become an efficient fat burner, you minimize the oxidative stress placed on your mitochondria, which is key.

The Importance of Meal Timing

Know's book also addresses the issue of meal timing. He does an excellent job of explaining what happens when you eat too late in the evening, when your body doesn't need the energy. In short, eating shortly before bed is one of the worst things you can do to your mitochondria. Know explains:

> *"This goes back to what causes damage at the level of the mitochondria, and one of those is excess calories. [F]ood is converted at the cellular level into electrons… and the electron transport chain essentially pumps protons into mitochondrial space.*
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> *We build up that concentration of protons [that] eventually flow back through ATP synthase and create ATP. In order for the ATP synthase to continue to run, it needs the building blocks of adenosine diphosphate (ADP). It takes a phosphate ion and combines [it with ADP] to create ATP. The thing is, we need to use up that ATP.*
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> *When you use up ATP your body breaks off that third phosphate and creates ADP again. That cycle can happen over and over again, as long as you're using*

up that ATP. The problem is, especially at night, when you … will be sedentary for the next eight hours … you're building up ATP but you're not using it. You're not breaking it down to ADP, so … ATP synthase basically shuts down. It doesn't have the building blocks of ADP anymore.

[T]hen, the entire chain backs up. The electrons cannot flow through the electron transport chain, protons aren't being pumped anymore, but because you ate late in the day, all those electrons are continuing to flow into the mitochondria and continue to enter the electron transport chain …

… (Basically, you have a mismatch of supply versus demand), you generate an excess amount of free radicals that will spill out and damage the mitochondrial DNA… [T]he entry into the electron transport chain [at complex I] is the No. 1 site of endogenous free radical production in your body."

An important side note to this is that excess carbohydrates, in particular, result in this backup of electrons, causing the production of superoxide. While not a pernicious free radical in and of itself, if you have high iron levels — which is far more common than low iron — combined with high superoxide, it produces hydroxyl free radicals, which is one of the most harmful.

The chemical reaction that creates these hydroxyl free radicals is known as the Fenton reaction. While you certainly need enough iron, having too high an iron level can cause severe damage, and this is one way in which it does that.

Why Some Populations Have Higher Exercise Requirements

Mitochondrial uncoupling is another interesting phenomenon that involves the flow of electrons in the electron transport chain. Certain populations, especially those from tropical and subtropical areas like Africa, are genetically predisposed to this problem and need to take steps to counteract it through proper diet and exercise. Mitochondrial uncoupling ties into brown fat or brown adipose tissue.

When hydrogen ions flow back through ATP synthase, energy is created. But in some cases, and in certain tissues, such as in brown adipose tissue, this process can become uncoupled. Instead of the hydrogen ions flowing back through ATP synthase, they flow through a different channel, creating heat rather than energy.

A benefit of this is that it allows the electron transport chain to continue to operate even though you're not using up energy. The hydrogen gradient is being dissipated through the generation of heat instead.

> *"The great thing with this is that when you have sufficient brown fat … you have a far lower risk of cardiovascular disease, diabetes and all sorts of different degenerative diseases because you're allowing those hydrogen ions to flow back without backing up the electron transport chain,"* Know explains.
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> *"Certain populations, like those that live in the far north, have quite a large amount of brown fat and that's because brown fat generates heat. That helps them stay warm in colder climates.*
>
> *On the other hand, populations that have originated from the equatorial regions typically have very tight mitochondria; they don't have a lot of uncoupling. This is one of the reasons why certain populations have a much higher risk of cardiovascular disease and obesity.*
>
> *[In these populations] it becomes increasingly important to ensure that the energy being produced… is constantly used up through physical activity and exercise. Not to say that that's not important for populations that live in the far north, but they have other mechanisms built into their bodies that allow them to produce less free radicals, or allow those electrons to flow through without having to have as much exercise."*

If you're not genetically predisposed to having higher amounts of brown adipose tissue, you have the capacity to make it. By exposing your body to cold temperatures on a regular basis (a process called cold thermogenesis), you will over time build more brown, heat-generating fat.

So, to summarize, if your genetic heritage stems from equatorial regions and/or you have very dark skin, you will tend to have less brown fat, and hence less mitochondrial uncoupling, which raises your risk of chronic disease. To counteract this biological reality, you will need to exercise regularly. Also, be mindful of your vitamin D level, and seriously consider regularly engaging in cold thermogenesis exercises to build brown and beige adipose tissue.

Practical Strategies to Optimize Your Mitochondrial Function

Thanks to living in a toxic environment, feeding your body inappropriate fuel, eating at the wrong time and not exercising enough, most people have less than optimized mitochondria. The good news is there are many ways to improve your mitochondrial function. As explained by Know, the two best and most researched ways to optimize mitochondrial function are exercise and calorie restriction.

> *"Exercise has been shown to upregulate genes like PGC-1 alpha. It also helps upregulate other nuclear gene factors like Nrf2. These are genes that … help your mitochondria become more efficient, [and] help them grow and divide so that you actually have more mitochondria.*
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> *I'm going to simplify it here, but the reason you end up with benefits to the mitochondria is that when you are physically active, you place an increased energy demand on your cells.*
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> *In response … free radicals signal that you need more mitochondria. So, your body adapts to physical activity by the mitochondria dividing and becoming more efficient. The next time you do some physical activity, it's less strenuous.*
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> *You have a greater capacity to generate the energy needed to meet that demand. That also means that the workload of whatever the cell needs to do at rest is now shared amongst a greater number of mitochondria.*
>
> *Each mitochondrion is now under considerably less stress, and therefore generating far fewer free radicals. That's one of the reasons why physically fit*

individuals have a lower risk of pretty much all degenerative diseases, including cancer, as well as a longer life span."

The Energy Demands of Relaxation

Paradoxically, not only does relaxation require energy, it actually requires far more energy than exertion. We typically associate energy input with strain. When you contract a muscle, you're straining the muscle, and we think of that as requiring energy. At the biochemical level though, during exertion, ATP is needed only at one site. A single ATP energy molecule is needed to bind to a protein called myosin to cause a contraction. This is called cross-bridge cycling.

During relaxation, however, two sites require ATP. You need an ATP molecule to bind to a receptor on calcium-magnesium-ATPase, which pumps calcium out of the cell, thereby initiating relaxation. A second site on that enzyme also requires an ATP molecule, but it doesn't have a high affinity for ATP.

The only way a second ATP can fit into that receptor is to have a large concentration of ATP, with the hope of one falling into place. In other words, while contraction takes just one ATP, relaxation actually requires hundreds of ATP molecules, and this has implications for your heart and cardiovascular health in particular. Know explains:

"We actually need to generate a significant amount of energy for our muscles to relax. That's a difficult concept to understand, but the easiest scenario that I can use to describe it, and I mention this in my book, is rigor mortis. When we die we're not producing any energy anymore, and our muscles go into a permanently contracted phase. They can't relax because there's no energy.

For a living person, this can cause a number of different health conditions associated with left ventricular hypertrophy or dysfunction as well as things like hypertension. When we're talking about the heart, what we call the ejection fraction is considered the measurement of heart function. So, when we have a small amount of ejection fraction, we're setting ourselves up for heart failure.

The ejection fraction is the percent of blood that the left ventricle pumps with each heartbeat. When it relaxes, that's the reference point of 100%. When it contracts, the percent of blood pumped out is the ejection fraction. What's normal is 50 to 70%; anything under 35% is considered an emergency situation. Of course, we want the heart to be able to relax as much as possible so it can have a greater volume to pump.

If the heart is not able to produce the energy it needs to fully relax, it partially relaxes, and then when it contracts, very little blood is pumped out … Essentially, what's going to happen is that the heart compensates by thinking it needs to grow more muscle.

[T]he ventricle walls in early stages of heart failure start to thicken because the heart inappropriately interprets that signal as not [being] strong enough. That sets up further complications that eventually lead to congestive heart failure."

Helpful Supplements

The same applies to your blood vessels, which are lined with tiny muscles that help regulate your blood pressure. When there's insufficient ATP to allow the blood vessels to relax, you end up with hypertension. This is in part why supplements like CoQ10 (ubiquinol) and magnesium help lower blood pressure, as both of these are intimately involved in the energy production process.

As detailed by Know, "Having an excess amount of CoQ10 is, at this point, seen to be a fairly effective therapeutic strategy to ensure [well]-functioning mitochondria." Aside from that, CoQ10 is a powerful fat-soluble molecule that prevents the oxidation of cholesterol. So, having sufficient amounts of CoQ10 prevents cholesterol from becoming troublesome. It also acts as a signaling molecule and helps protect cell membranes from damage.

Pyrroloquinoline quinone (PQQ) is a vitamin-like substance and a cousin to CoQ10. PQQ helps with mitochondrial biogenesis. As I mentioned earlier, the greater number of

mitochondria you have, the more energy your cells are able to produce, and the better they function overall. So, having sufficient amounts of PQQ encourages the proliferation of mitochondria.

According to Know, “CoQ10 and PQQ are both very important nutrients for mitochondria health, but of the two, I would definitely say CoQ10 is still the more important one.” For adults, the reduced version of CoQ10, called ubiquinol, is a better choice as it’s more absorbable. Magnesium also plays a really important role.

The Benefits of D-Ribose

D-ribose is another supplement that can be quite useful, as it's required by ADP.

> *"D-ribose is a five-carbon sugar, and it's completely safe to consume even for diabetics because it has no impact [on] blood glucose. [R]ibose … gets into the cells and converts into the adenosine base … which goes on to have the phosphate ions attached to it to create ADP and ATP.*
>
> *The importance of D-ribose as a supplement is that even though our bodies produce D-ribose on its own, it's a very, very slow process.*
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> *… It's probably the rate limiting factor in recovery for cardiovascular patients, people with chronic fatigue … stroke and heart attack … D-ribose is incredibly important, probably one of the most important nutritional components for a subgroup of individuals that are suffering from heart attack, stroke and/or chronic fatigue."*

D-ribose is nontoxic and is virtually impossible to overdose on, and if you've suffered a stroke, heart attack or struggle with chronic fatigue, it's a really important supplement to include in your regimen. Taking D-ribose prior to cardiac surgery can also help minimize damage associated with reperfusion injury. Since most people have some degree of mitochondrial dysfunction, it may also be helpful for general health, especially if you exercise regularly.

"The minimum therapeutic dose is typically around 5 grams, and some studies have used 10 or even 15 grams. I would say 3 to 5 grams is the minimum, but if you get anything, it's going to better than nothing," Know says.

"I also think it would be great for individuals going through any sort of low-carb program to supplement with D-ribose, because typically what happens is that our bodies use glucose as a starting point to create D-ribose, but that is a very slow process.

In a situation where you're really cutting out glucose, your body is going to shift any spare glucose that it has into serving other purposes, so it might take a long time to rebuild any purine or energy pool in the absence of D-ribose supplementation. Especially for anyone going through [nutritional] ketosis, I think D-ribose is definitely something to consider."

More Information

While we covered a lot in this interview, there's plenty more in "**Mitochondria and the Future of Medicine: The Key to Understanding Disease, Chronic Illness, Aging, and Life Itself**." Considering mitochondrial health underpins health and longevity in general, the information in this book is invaluable. So, to learn more, be sure to pick up a copy.