

Transforming Health — How to Navigate Reductive Stress and the Metabolic Impact of Dietary Fats

Analysis by [Dr. Joseph Mercola](#)

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STORY AT-A-GLANCE

- › Reductive stress, caused by an excess of electrons in the electron transport chain, decreases metabolism and leads to degenerative diseases
- › Dietary fats, particularly the balance of saturated and unsaturated, have a direct influence on your metabolic rate and health
- › Desaturase enzymes, which are affected by dietary fats, signal your body to adjust its metabolic rate for energy conservation
- › High consumption of polyunsaturated fats (PUFAs) mimics signals for metabolic slowdown, thereby contributing to metabolic syndrome
- › Strategies to improve your metabolic health include managing your dietary fat intake and understanding the role of specific nutrients like stearoylethanolamide (SEA) in counteracting the negative effects of monounsaturated fats, particularly oleic acid. These fats are implicated in slowing down the metabolic rate and increasing reductive stress, which SEA helps to mitigate by influencing metabolic processes and reducing inflammation

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In this interview, repeat guest Brad Marshall, a molecular biologist, explains how different dietary fats influence your metabolism and overall health. You may want to listen to this interview a couple of times. If you still find it hard to understand, copy and

paste the corresponding sections of the transcript into ChatGPT and ask it to explain it to you in even simpler terms.

In our previous interview, Marshall explained **reductive stress** and how it causes damage that leads to virtually every degenerative disease and the most common causes of death. Molecular biology can be hard to understand which is why I created the best 2-D illustration of how your body creates cellular energy. It will be helpful for you to review this illustration during our discussion.

 excess fat lowers nad+

The other strategy that will help you learn this important information is to have a dialog with ChatGPT 4 or your favorite large language model and ask it to help explain any concepts you don't understand. If the answer is something you still don't understand ask Chat to simplify its answer. Continue asking questions so you understand everything.

In summary, reductive stress results from an excess of electrons that slow down your metabolism and energy production. It's like your body's systems are overwhelmed with energy they can't properly use, which leads to decreased efficiency and damage over time.

Why is it so important to understand these concepts? Because they're the central keys to your health. If you understand these foundational concepts, you can make choices that will move you out of disease and towards health — because your body wants to be healthy. It's designed to be healthy and will achieve that automatically once you give it what it needs.

I've admired Brad's work so much that I've hired him to be my research director and we're developing a test to measure the redox potential of your body. At present, such tests are not commercially available, and those that do exist provide results that are questionable at best.

How Dietary Fats Affect Metabolism

As explained by Marshall, reductive stress and metabolic syndrome might be better understood through the lens of evolution and animal behaviors like torpor – a state of decreased metabolic activity.

Animals adapt by changing the types of fat in their bodies seasonally to prepare for periods of dormancy like hibernation. The thing that triggers this fat composition change is the composition of fats in the animal's diet.

For instance, the consumption of insects with high saturated fat content indicates to mammals the need for a more active metabolism suitable for warmer climates. Conversely, diets high in monounsaturated fats signal the approach of winter, prompting animals to lower their metabolic rate in preparation for hibernation.

Key components of this process are desaturase enzymes, which are responsible for adjusting the types of fats within your cells. These enzymes – Delta-6-desaturase, Delta-5-desaturase, and Delta-9-desaturase – signal your body to slow down its metabolic rate in anticipation of periods when less energy will be required or available by converting saturated fats into unsaturated fats, including monounsaturated fats.

As animals approach colder months, they naturally increase the production of these desaturase enzymes. This increase leads to a higher concentration of monounsaturated fats in the body, which is more efficiently stored as fat. This accumulation is part of the body's preparation to conserve energy and maintain survival during periods of scarcity.

Thus, you could say that desaturase enzymes act as a metabolic switch that turns on your body's torpor mode. By modifying the fat composition within your body, they effectively lower your metabolic rate, thereby allowing your body to conserve energy.

And again, this switch is influenced by the type of fat you consume. Saturated fats are associated with a higher metabolic rate and less reductive stress, while monounsaturated and polyunsaturated fats (PUFAs) lower your metabolic rate and increase reductive stress.

In short, if you consume high amounts of PUFAs, you're tricking your body into thinking you need to conserve energy for hard times, like a famine or long winter with scarce food supplies. This process of conservation, in turn, downregulates or shuts down various biological processes because your body doesn't have enough energy for all of them.

Why LA Is So Destructive

While we typically don't think of torpor applying to humans, most Americans are in this state. The increase in unsaturated fats in the human diet over the last century — particularly PUFAs — mimic the natural signal for animals to enter a torpid state, but since humans do not hibernate, this reduced metabolism is neither necessary nor healthy. The process is further exacerbated when these fats become oxidized, as this increases reductive stress.

"In the last 100 years, we've eaten more and more and more of these unsaturated fats," Marshall says. "And, of course, the polyunsaturated fats contribute to this process as well because the Delta-6-desaturase is the limiting step in the oxidation of the polyunsaturated fats."

You've talked a lot about concerns with polyunsaturated fats, and what I see when I look at it is, linoleic acid (LA) ... is okay if it stays as linoleic acid, but once it starts getting converted to oxidized fats, that's when it becomes a real problem."

Through a series of enzymatic steps, LA is transformed into arachidonic acid. Arachidonic acid, when oxidized, can form various types of hydroxyeicosatetraenoic acids (HETEs), which are signaling molecules involved in numerous physiological processes, including inflammation and the immune response.

Marshall believes that two HETEs in particular, 5-HETE and 12-HETE, control the shifting of metabolism towards torpor metabolism. These HETEs, in turn, appear to be controlled by highly destructive oxidative linoleic acid metabolites (OXLAMs) that are produced

when LA is oxidized.

The Link Between High-PUFA Diets, Metabolic Syndrome and Related Issues

When you oxidize a lot of PUFAs you also activate a nuclear receptor called the aryl hydrocarbon receptor (AHR), which controls your circadian rhythm. Marshall comments:

"If you give a mouse a drug that strongly activates the aryl hydrocarbon receptor, it shuts down the circadian rhythm of the mouse. The aryl hydrocarbon receptor controls your circadian rhythm. And people who have metabolic syndrome have issues with sleep.

If you trigger the aryl hydrocarbon receptor, you also get a dysregulated gut microbiome. If you are oxidizing a lot of polyunsaturated fat, you activate the aryl hydrocarbon receptor and all of a sudden you have overgrowth of bad gut bugs and you'll have a decrease in the good gut bugs."

The reason why AHR activation catalyzes a transition from beneficial to pathogenic gut bacteria is because the AHR is highly involved in controlling the immune system. If you activate the AHR, you see an increase in myeloid derived suppressor cells — immune cells that suppress your immune response.

Are Starches Good or Bad? It Depends

At this point in the conversation, Marshall brings up a crucial point. Many in the Ray Peat community believe that starches, especially resistant starches, will promote the growth of pathogenic bacteria that produce endotoxin, also known as lipopolysaccharide or LPS. LPS can get into your bloodstream and cause all kinds of problems, so you don't want a high LPS response.

However, after looking at this issue for the last 18 months, I've started to understand the flaws in Peat's work. One of the primary functions of the gut is to maintain an anaerobic environment (an environment without oxygen). The problem is, you need energy to keep oxygen out of there, and if that energy is not available, oxygen is going to seep in.

Most beneficial bacteria are gram-negative, and they're called obligate anaerobes. They do not have LPS in their cell wall and hence will not produce endotoxin when they die off. However, when you don't create enough cellular energy you are unable to create a low oxygen environment in your large intestine.

This kills the beneficial bacteria as oxygen seeps in and they are unable to survive. When they leave, they create a hole that allows endotoxin-producing bacteria — facultative anaerobes — to take over through competitive inhibition. Facultative anaerobes can tolerate oxygen and survive.

The primary obligate anaerobic bacterium in your gut is a species called Akkermansia, which makes mucin, the protective layer in your gut. When your Akkermansia die off due to lack of cellular energy to maintain the proper oxygen gradient in the large intestine, then your mucin barrier starts to break down and you end up with leaky gut.

Now, the reason starch CAN be problematic is because, if you are metabolically inflexible (and most are), then you're not making enough mitochondrial energy to maintain a healthy gut. So, the idea that starch is problematic is likely true for most people, because most people have a disrupted microbiome. Starch is indiscriminate and will feed any bacteria. So, since most people have a preponderance of pathogenic gut bacteria, starch causes problems.

The flip side of this is that if you have a healthy microbiome, starch can be quite beneficial. So, the primary goal is to get your cellular energy up and improve your microbiome first. Then you can eat starch.

I now eat about 1.5 pounds of white rice a day and have cut down on my fruit consumption. In total, I consume over 500 grams of carbs a day, but I now get less fructose (as starch doesn't contain fructose like fruit does). Ultimately, I suspect starch

may be the ideal fuel once your microbiome is optimized. But again, it's all dependent on your gut health.

I also added over 50 grams of collagen from homemade bone broth per day and added raw milk cheese with animal rennet. This experiment has resulted in gaining 4 pounds but my percent body fat dropped from 8.5% to 6.5%. So, I gained over 4 pounds of muscle and no fat. That's a good trade from my perspective.

Other Feedback Loops That Push Us Toward Metabolic Syndrome

While Marshall agrees with my theory of why starches can cause problems, he points out that there are other feedback loops at work as well:

"This is all part of one sort of big complicated positive feedback loop. I 100% agree with you about the gut barrier function. But I also think that there's a whole bunch of aligned systems that are pushing us towards this outcome [metabolic syndrome]."

When you look at the hibernating animals, when they go towards winter and you see all those desaturase enzymes are increased, their gut permeability increases. One of the tricks that the animal does as the hibernating season is approaching is they increase gut permeability, and they let more LPS in.

That may also let more oxygen through. I'm not sure. One of the patterns that you see in obesity and metabolic syndrome is that branched-chain amino acids in your bloodstream increase and glycine goes down. In mice, if you supplement with glycine, it increases gut barrier function.

So, you have this pattern going into winter where AHR is activated, desaturases are activated, gut barrier function is decreasing and LPS is coming in that causes release of CD38, [which] breaks down NAD⁺. And so, anytime LPS is coming through, it's decreasing NAD⁺ availability.

The thing about that is, all three desaturases run off NADH and not NAD+. So, the gut inflammation leads to increased activity of these desaturases, which leads to increased monounsaturated fat production, which continues to push you further in that direction of reductive stress, which lowers glycine, which makes the gut leakier. To me, it looks like it's all wrapped into the same process.

These processes all work together, and they all work in these feedback loops because if you are an animal in the right situation, you want to have a low metabolic rate, you want to have slow metabolism, and you want to be storing extra fuel.

It's a very complicated process with a lot of different parts, and they're all working together to achieve the outcome, which we call metabolic syndrome. Because in our situation, we don't have to store extra fat for winter and we're not going to hibernate."

Tracing the Inflammatory Cascade to Its Root

Marshall also points out research showing mice that lack SCD1, and therefore cannot make monounsaturated fat, have very low inflammatory markers.

In autumn, hibernating animals increase SCD1, which increases production of monounsaturated fats, which in turn increases the inflammatory immune cells like TLR4 and NF kappa beta. At the same time, stearoylethanolamide (SEA) production is reduced. SEA is a bioactive lipid made from stearic acid that is noted for its effects on reducing appetite and inflammation.

However, if you decrease Delta-9 desaturase activity, you eliminate that whole inflammatory cascade. So, Marshall suspects that it's the inflammatory cascade resulting in elevated C-reactive protein can be traced back to the activation of Delta-9 desaturase. Hence, the remedy needs to include the deactivation of Delta-9 desaturase.

SEA, which is available as a supplement, has the remarkable effect of drastically raising your metabolic rate if the negative feedback loops just described are in play. In animal studies, SEA has been shown to reduce inflammation, suppress production of TNF alpha, SCD1 and Delta-9 desaturase.

“So, it's doing all of the things that you would predict would help your metabolic rate,” Marshall says. In the interview, he describes the effects his SEA supplement had on his [morning body temperature readings](#), which is a simple way to gauge your metabolic rate, and how he was able to use that to fine-tune his dosage.

What Do Countries with Low Diabetes Rates Eat?

As noted by Marshall, West Africa has one of the world's lowest diabetes rates, partially attributed to its diet, which is rich in starchy tubers like plantains, cassava, and African yams, as well as collagenous meats like beef skin. These foods are often used in stews, extracting collagen and gelatin.

This dietary pattern, emphasizing starchy tubers and collagen-rich meats, contrasts with diets higher in processed foods and may contribute to the region's lower diabetes prevalence, which is below 3%.

My idea of a healthy meal would be white rice cooked in bone broth, topped off with a couple of egg yolks and a small amount of beef liver. This meal would be high in starch and collagen, and low in fructose and muscle meat, which has a very different amino acid composition than collagen. For a refresher on the difference between muscle meat and collagen, see “[Why Collagen Is a Proven Necessity](#).” Marshall comments:

“One of the things about starch is, if you eat a bunch of starch, your NAD+ availability increases postprandially. After the meal, you have more NAD+ availability if you're burning a lot of starch. And so, it all comes down to reductive stress.”

Why Olive Oil Isn't as Healthy as It's Made Out To Be

Marshall also recounts research showing the differences between saturated and unsaturated fats in terms of how they affect your metabolism.

"This experiment has been done in humans about four or five times. They feed people bread and butter or bread and olive oil, and measure how much oxygen they're consuming and how much carbon dioxide they're breathing out. That's called respiratory exchange ratio.

If you look at those two numbers, you can determine how much carbohydrate and fat people are burning. And so, if people eat bread with butter, they'll have a relatively high respiratory exchange ratio, and that means that they're burning a lot of the carbohydrate in the meal. So, you eat bread and butter, you can burn that carbohydrate cleanly, which is the right way to do it.

If you eat bread and butter, you want to burn those carbs first. Then, as your blood glucose levels drop, then you'll start to burn more of the fat from the meal. That's the correct sequence. If you eat olive oil and bread, you burn less of the glucose right away.

I would argue that the olive oil makes you essentially acutely insulin resistant. Because the insulin, you eat that bread, the insulin is signaling, it's trying to clear the other things out to allow that glucose to burn. But if you eat bread and olive oil, your respiratory exchange ratio will be lower, and that means you're burning more fat.

And of course, if you read those articles, they say, 'Oh, eureka. If you eat olive oil, you'll burn more fat than if you eat butter.' When I look at that, I say, 'This is bad. This is not what you want.'"

Olive oil, if pure (and most aren't) is mostly oleic acid, a monounsaturated fat, but PUFAs have the same effect. Both will inhibit glucose metabolism. What's more, when you consume oleic acid, it creates oleoylethanolamide (OEA), which has the opposite effect of SEA.

OEA activates a nuclear receptor called PPAR-alpha, which directly turns off glucose metabolism. So, every time you eat monounsaturated fat, PPAR-alpha is activated and turns off your ability to break down glucose.

High Metabolism Is the Goal

Marshall continues:

"If you compare bread and butter to bread and olive oil, the bread and butter looks like that's what you want ... as you want to burn those carbs. Because if you burn those carbs, your NAD+ availability will go up. And I said this in the last show, but there's this old saying that 'fat burns in the flame of carbohydrate.'

You get that NAD+ availability up and you get that flywheel spinning, and now you can efficiently burn the fat in the meal and also your stored body fat, because the carbs are really driving that process."

One way to accomplish that is by taking a SEA supplement, as that will increase your metabolic rate. Remember, the key goal is to increase your body's ability to create cellular energy, which means improving your mitochondrial function and increasing your metabolic rate. If you can do that, it doesn't matter what disease you have; most will begin to improve.

Again, to summarize, SEA helps counteract the effects of oleic acid by influencing your body's metabolism and its response to fats. It does this, in part, by suppressing the enzyme delta-9 desaturase in the liver, which plays a role in converting saturated fats into monounsaturated fats like oleic acid.

By doing so, SEA helps reduce your body's tendency to store fat, mimicking a condition where energy storage for winter is unnecessary. This, in turn, helps to improve your metabolic rate and reduce inflammation by affecting NF kappa beta, a protein complex involved in inflammatory responses.

Lab Test for Redox Status Is in the Works

As mentioned earlier, Marshall and I are developing a lab test to assess redox status by analyzing three pairs of compounds: lactate and pyruvate, acetoacetate and beta-hydroxybutyrate, and oxidized and reduced glutathione.

We believe this approach will offer more precise insight into cellular health than directly measuring NAD⁺. We want this test to be affordable and able to provide detailed information about your mitochondrial function to help you monitor your progress as you make various lifestyle changes.

In the interview we discuss, in detail, how and why evaluating these three redox pairs are crucial for understanding how your body processes fuel and manages oxidative stress. We also explain how the balance of these pairs in the mitochondria and cytoplasm can indicate overall metabolic health and the effectiveness of your body's antioxidant defenses, such as glutathione.

In short, the test aims to provide insight into your mitochondrial function and how it can be overwhelmed by excessive or improper fuel intake, which has significant implications for your health.

Marshall also explains how antioxidants, like vitamin C, interact with free radicals, substances with unpaired electrons that can damage cells. When antioxidants donate an electron to free radicals, like superoxide or lipid peroxides, they neutralize them, preventing damage.

However, this process can be complex, as illustrated by glutathione, a crucial antioxidant that, when in its reduced form, helps eliminate harmful substances but can also indicate reductive stress in cancer cells. Thus, maintaining a balanced level of reduced glutathione is essential for health.

More Information

To learn more, please listen to the interview in its entirety. You may need to listen to it several times, even, to really understand it. Once you do, however, the answers to many of your health problems will become that much clearer. And, if you want to dive deeper into molecular biology, be sure to check out Marshall's YouTube channel, [Fire in a Bottle](#). Marshall also sells a SEA supplement that is available at [his website](#).

The Best Nutrition Course Is NOW Available for You!

In closing, I have other good news. Shortly, I will be sending out invites to train individuals interested in becoming one of my health coaches. My health coaches will be some of the best trained coaches on the planet because they will understand how biology works and how to correct it to optimize health.

Many will apply but only a few will be accepted. Once they are accepted, they will be allowed to enroll in my nutritional biochemistry course at no charge. This course is based on the concepts of the late Dr. Ray Peat who popularized bioenergetic medicine. That's a fancy word for optimizing diet choices to maximize cellular energy production.

Poorly functioning mitochondria is pervasive and probably exists in 98% of the population. Diligent application of the principles outlined by Peat will help your mitochondria recover so they can produce the amount of energy they were designed to. This is important because your body needs energy to activate its intrinsic healing capacity.

The foundation for the nutritional biochemistry course that will be taught to our health coaches is from a course that Ashley and Sarah Armstrong put together. In my view, it is the best health course I've ever seen.

I only wish I had had this course when I first started practicing medicine. It would have been a game changer. It's hard to imagine how many additional hundreds of millions of people I could have helped with this knowledge. Not to worry though, as the knowledge is now available for you.

If you are seriously interested in understanding how your body works, and more importantly, what specific actions you can take to guide it to working the way it was designed to, then [this is the course you need to take](#).

You can enroll for the course on their website. I take no commissions from recommending this course. All the funds go directly to the Armstrong sisters. They're probably the most knowledgeable farmers on the planet when it comes to health. This is why they can produce some of the healthiest food possible. But you may realize that farmers don't earn very much, so you can support their mission to provide the world with healthy food by [purchasing their course](#).

I would encourage you to seriously consider taking advantage of the wealth of knowledge that has taken them many years to compile and make available to you in an easy to learn format.