

### **How to Conquer Fatigue and Low Energy**

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#### STORY AT-A-GLANCE

- > To address fatigue and low energy, you need to improve your mitochondrial energy production
- Mitochondria have a mutually exclusive dual function. They produce energy, but they're also environmental sensors that detect threats inside the body. When a threat is detected, the mitochondria downshift energy production to focus on self-defense
- > Common threats that can result in reduced mitochondrial energy production include oxidative stress, poor nutrition, environmental toxins, psychological stress and sleep deprivation
- Mitochondrial capacity declines by about 10% with each decade of life, but it's not a natural function of aging. Rather, the loss of mitochondria is due to a lack of hormetic stress. Mitochondria have to be challenged and stimulated in order to stay big and strong
- Light deficiency is an extremely common cause for fatigue. Sun exposure is required for melatonin production in your mitochondria, which protects them from damage. Red and infrared light also stimulate tissue-specific growth factors, directly stimulate ATP production at the mitochondria level, and act as signals to encourage mitochondria to grow bigger and stronger

In this interview, Ari Whitten, a return guest, discusses his latest book, "Eat for Energy: How to Beat Fatigue, Supercharge Your Mitochondria, and Unlock All-Day Energy."

Whitten has also written an excellent book about infrared light exposure or photobiomodulation as a healing modality, called "The Ultimate Guide to Red Light Therapy: How to Use Red and Near-Infrared Light Therapy for Anti-Aging, Fat Loss, Muscle Gain, Performance, and Brain Optimization."

As you might guess, the focus of his latest book is fatigue, and the foundational core for addressing that is to improve mitochondrial energy production. Your circadian rhythm also plays an important role. Whitten explains the premise of the book:

"It's a collection of science-based strategies as far as what to eat, how to eat and when to eat, that can be tied in with any particular dietary pattern that you've already adopted. So, I'm not asking if you're paleo or vegan or keto or Mediterranean. I'm not asking you to change that.

It's dozens of strategies that you can incorporate into the dietary pattern of your choosing. So, I feel like it's a really key piece of the puzzle for a lot of people.

They can just immediately plug in with pretty minimal effort and get big results ...

In the last 100 years, we've seen massively accelerating risks of dozens of diseases, and that is not the result of everybody being a unique individual and responding randomly to what's going on. It's not that everybody's genetics just decided to express lots of disease.

It's because the modern world changed in very fundamental ways, as far as diet, the modern lifestyle, as far as being sedentary, being in climate-controlled offices, losing all these forms of hormetic stressors, sleeping less, disrupting our circadian rhythm — these are the main drivers of pretty much all of these different chronic diseases.

And the answer isn't to treat everybody as a unique individual and pretend like we don't know all of these universal factors that are the actual root cause drivers of these diseases. It's to address the foundation of these root cause drivers of diseases. That's where you have to start."

### A New Understanding of Mitochondria

In high school and college biology courses, we're taught to think of mitochondria as mindless energy generators that take in the food we eat, mostly carbs and fats, and then pump out cellular energy in form of the ATP. However, in the past five to 10 years, we've gained a whole new understanding of mitochondria, largely thanks to the work of Dr. Robert Naviaux, who runs a mitochondrial medicine lab at the University of California, San Diego.

"Naviaux, I think, is one of the most brilliant scientists and has created one of the biggest breakthroughs in medicine in the last century, arguably. He figured out that mitochondria have a second role, other than energy production, and that is in cellular defense.

In his words, mitochondria are the central hub of the wheel of metabolism. They are not just energy producers, but also environmental sensors, and they are constantly sampling the environment around them, figuring out what's going on in the body.

And, basically, they're asking one fundamental question: Are we under attack? Is there something we need to defend against? And this is the big key — these dual roles of energy production and cellular defense are mutually exclusive. So, to the degree that mitochondria are picking up on some dangers that are present, they turn down the dial on energy production.

And if the mitochondria are turning down the dial on energy production, subjectively on a macro level, us as an organism, a collection of trillions of these cells filled with mitochondria, feel the symptom of fatigue. We can think of our energy levels as largely a function of the degree to which our mitochondria are detecting the presence of dangers or threats in the body."

Common threats your mitochondria might be responding to if you feel fatigued include oxidative stress, poor nutrition, environmental toxins, psychological stress and sleep deprivation, just to name a few.

#### What's Your Resilience Threshold?

Most if not all stressors can be boiled down to oxidative stress, reactive nitrogen species, inflammation and purinergic signaling (a situation in which energy molecules leak out of the cell). Even something like psychological stress can cause this kind of reaction. But whether the stressor is serious enough to cause fatigue depends on your resilience threshold. What wipes one person out might not affect another.

"I like to think of fatigue as having two fundamental causes," Whitten says. "One is all of these different kinds of environmental and lifestyle stressors. The other thing that interplays with, and is often left out by a lot of people, is what is happening at the cellular level inside of your body.

And the key thing to understand here is that our cells can either be filled with big, strong mitochondria, and lots of them, or weak, fragile, shrunken, broken, dysfunctional mitochondria, and very few of them.

It's been shown in research that mitochondrial capacity declines by about 10% with each decade of life. If you look at older people, they generally have somewhere between 50% to 75% lower mitochondrial capacity than a young person.

But it's not a natural function of aging, because we know from other research that when they look at mitochondrial capacity of healthy 70-year-olds, who are lifelong athletes, they don't have lower mitochondrial capacity than an adult at 40 years old.

What that tells us is the loss of mitochondria is not a function of aging, per se. It's a function of lack of hormetic stress in your life. Mitochondria have to be challenged and stimulated in order to stay big and strong."

# **Other Factors That Influence Your Energy Levels**

While mitochondrial dysfunction is a central issue in fatigue, other factors also come into play, including:

- Low muscle mass Greater muscle mass contributes to metabolic flexibility and health, because muscle acts as a sink for glucose, thereby reducing your risk of insulin resistance. Low muscle mass, on the other hand, is a leading contributor to early death, and it's a major contributor to low energy and fatigue
- Elevated blood sugar and insulin resistance This primarily goes back to a poor diet high in processed foods and constant grazing throughout the day. Eating a whole food diet and implementing TRE can go a long way toward normalizing your insulin and blood sugar
- Lack of hermetic stress such as insufficient amounts of exercise
- Stress
- Poor gut health

#### **How Your Diet Influences Your Energy Level**

Naturally, your diet has a central influence on your energy level. One key driver of low energy and ill health is excessive omega-6 linoleic acid (LA) intake. LA contributes to insulin resistance, obesity and chronic inflammation, and as mentioned earlier, when mitochondria detect inflammation, they dial down energy production to shift resources toward self-defense.

High LA consumption has also been implicated in neurodegenerative diseases, cancer and many other chronic diseases. Processed food, which is not only high in LA but also sugar, can also considerably impact your energy levels by impairing your hormone regulation.

## **Circadian Rhythm Disruption Is a Common Culprit**

According to Whitten, arguably one of the most important things you can do to improve your energy level is to optimize your circadian rhythm by consistently going to bed and rising in the morning at the same times. Another crucial factor is to get plenty of daytime sunlight exposure and to minimize artificial light exposure at night. As explained by Whitten:

"The circadian clock in your brain learns to distinguish what is day and what is night based on the differences in light intensity, along with the color of the wavelengths of that light. When you start your morning in indoor environments, under indoor lighting, looking at screens, and end your day in indoor environments with indoor lighting, looking at screens, you don't have a big [light intensity] differential."

Your circadian rhythm is also influenced by nutrient sensors throughout your body. While you use light to optimize the central clock in your brain, you use nutrition to optimize the peripheral clocks and sync them with the central clock. One way to do this is through time-restricted eating (TRE), where you eat all your meals within a six- to 10-hour window.

#### The Importance of Sun Exposure

Light deficiency is another extremely common cause for fatigue. Sun exposure triggers vitamin D production, which is important, but it also has many other functions and benefits that can directly impact your energy level.

For example, the vast majority of melatonin, some 95%, is produced in your mitochondria in response to sunlight (specifically red near-infrared light, which is what provides warmth). Melatonin is a potent anti-inflammatory, so sunlight allows you to target oxidative stress right where it's needed the most.

"Melatonin is absolutely vital for protecting your mitochondria from harm and preventing them from accumulating damage as you age," Whitten says. But swallowing melatonin is useless for this, as oral melatonin cannot reach the mitochondria. 66 Red and infrared light directly stimulate ATP production at the mitochondria level. These wavelengths also create a transient increase in reactive oxygen species, which are signaling molecules that instruct the mitochondria to grow bigger and stronger. 99

Sunlight also allows for the conversion of retinol (vitamin A) to retinoids, which is crucial for the function of vitamin D, and interacts with your malanocortin system, which involves alpha-melanocyte-stimulating hormone that helps regulate inflammation and appetite.

Sunlight also creates a surge of nitric oxide, which helps normalize your blood pressure and reduce your cardiovascular disease risk. Whitten cites a Swedish study that showed women with the lowest sun exposure had a cardiovascular disease risk equivalent to smoking a pack of cigarettes per day. Red and infrared light also have a long list of other health benefits.

Importantly, red and infrared light directly stimulate ATP production at the mitochondria level. These wavelengths also create a transient increase in reactive oxygen species, which are signaling molecules that instruct the mitochondria to grow bigger and stronger.

Red and infrared wavelengths also stimulate tissue-specific growth factors. So, in muscle cells, it increases insulin-like growth factor 1, which is a key growth factor for muscle growth. In your thyroid, it stimulates growth factors that help regenerate thyroid gland tissue in the brain.

In your skin, fibroblasts are stimulated by red and near-infrared light to increase collagen production. So, essentially, red and infrared light act as signals that trigger growth and regeneration at the cellular level, throughout your whole body.

"Our biology has evolved for millions of years to require adequate sun exposure in order to express normal health," Whitten says. "Just to function normally, we require these different bioactive wavelengths and red and infrared light ...

We know that hermetic stress, that doing exercise, doesn't just protect the cells and the mitochondria from harm from exercise. It protects against a broad range of other stressors.

So, having a body that does exercise, that's fit, protects you from oxidative damage that might occur from psychological stress or sleep deprivation or environmental toxins — things that are totally unrelated to the initial source of that hermetic stress that led to those adaptations.

I think what we have with melatonin is probably something that's very similar.

This is something critical for protecting our mitochondria from a broad range of, basically, every type of stressor. You got to have those melatonin levels charged up, and that's a function of exposing your body to light."

#### The Antiaging, Energy-Boosting Benefits of Methylene Blue

Methylene blue is the parent molecule for hydroxychloroquine and chloroquine, an off-patent drug commonly used to treat not only malaria but also COVID-19. Interestingly enough, this molecule has been shown to have antiaging benefits when used topically. There's even a new cosmetics brand that uses it in their formulas. While it has a blue tint, when mixed with a carrier oil it does not stain your skin blue. According to Whitten, methylene blue:

"... has profound antiaging effects, anti-wrinkle effects and protects that skin from damage. It has mitochondrial protective effects ... it's neuroprotective, combats neurological disease and improves long-term brain health. It can also help increase energy ...

It's worth mentioning that there are some contraindications, there are some interactions with certain drugs that can be dangerous. Definitely, SSRIs [are

contraindicated]. There's also a strange medical condition called G6PD [that it's contraindicated for]."

Methylene blue also contains important copper enzymes called ceruloplasmin, which acts as a copper storage in your body. Copper is extremely important from mitochondrial energy production, and methylene blue forms a buffer to oxidation, which allows the copper to work better.

#### **More Information**

To learn more, be sure to pick up a copy of "Eat for Energy: How to Beat Fatigue, Supercharge Your Mitochondria, and Unlock All-Day Energy." The book addresses several foundational nutritional causes of fatigue and how to fix it, including:

The influence of your circadian rhythm and how to optimize it via nutrition

TRE and how to sync your eating window with your waking-sleeping cycle

Calorie stacking — how stacking more of your daily calories towards the earlier part of the day results in increased energy levels (in part by enhancing neurotransmitters and hormones that are synced with the circadian rhythm)

How to optimize your body composition

How to optimize your gut health

Superfoods and supplements to optimize energy levels

You can also learn more by tuning into his popular podcast, "The Energy Blueprint," where every week he delves into a wide variety of health promoting strategies.

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