How to Double Your Energy – Ari Whitten – #934

Dave:
You're listening to The Human Upgrade with Dave Asprey. Today we're going to talk about one of my favorite topics, it's about energy. Because there is a hidden epidemic of fatigue, which is a word I actually don't like because, I don't know, fatigue is one of those where I'm feeling fatigued, but really what we're talking about is, you are straight up tired, you have nothing left in the tank. And this is how I pretty much lived my life until I was 30 and I really figured out the bio hacking things. And chronic fatigue syndrome is where I was, which is the worst end of that. And studies are actually showing now that most people in the US have some level of just feeling tired as hell. The way I like to describe it is, you're driving, you have the accelerator all the way to the floor, you can push harder, but it's not going to do anything. And the car is going slower and slower and there's just nothing you can do.

It's not willpower. It's something else. So, we're going to talk about that. And I promised you that I was going to tell you what you're going to learn about so you can decide whether this is the right episode or whether to skip back one or forward one or whatever else, because there's a lot to learn and I do want to overwhelm you. I just want every second that you spend listening to this on 1.5x to be worth it for you. So, you're going to learn something about what's causing dysfunction in your mitochondria and how you can repair these, and you're going to learn about strategies that absolutely double your energy levels, things that are mitochondrial based. This is my favorite aspect of energy, and something that changed my life when I learned about mitochondria in 1997 and started working on my own. And we're going to learn from Ari Whitten, who's been studying and teaching natural health science for about 25 years, who also had chronic fatigue like I did. And he spent the last seven years working on human energy.

So, we're going to go through what he's learned about mitochondria, we're going to compare it to what I know about mitochondria, and we're going to have a mitochondria flex. And we're going to see who has the most mitochondrial techniques and which ones are better than the others. So, I want to learn things from Ari and I want you to learn things from him, too. But Ari, I'm going to ask you all sorts of hard questions, are you up for it?

Ari Whitten:
I am up for it. Yes.

Dave:
All right. It's going to be fun. Okay. You wrote a book on red light therapy. I think I would agree with you that's important. And you've talked about low carb diet traps in other books and even the low carb myth, because turns out you make energy from carbs. But let's just get right into it. Tell me about human energy, where it comes from.

Ari:
Yeah. Well, I mean, there's really a million different processes in the body that relate indirectly or directly to energy levels. I mean, we can talk about hormones, we could talk about thyroid hormone, we could talk about cortisol, we could talk about epinephrine and norepinephrine, we could talk about

testosterone, and all of these are impacting on variables related to energy production. We could also talk about neurotransmitters, we could talk about dopamine and serotonin and orexin. We could talk about so many different aspects that are tying into this energy puzzle, and the story could really go on endlessly in terms of that complexity. But at the core of it, I really see mitochondria as the most upstream thing that is regulating human energy levels.

I really see mitochondria as the most upstream thing that is regulating human energy levels. So, not just playing a role in some particular biochemical process that is indirectly related to energy production, but the actual thing that is deciding whether we should be producing lots of energy at the cellular level or not very much energy, that's what our mitochondria do. So, that's the short version of that.

Dave:
The most important thing that I think you said there is core to what I believe, which is that mitochondria aren't just power plants, they're smart power plants and smart manufacturers. They decide, not you. And then they either make energy or they make something else, like fat or inflammation, or whatever. So, according to your book, 5.4 million adults have chronic fatigue syndrome, but you think that the fatigue epidemic is more like a hundred times bigger, which would be a hundred times five, more than the US population. I'm not sure if I believe that, but okay. Well, let's go with 70, so we hit the US population. So, pretty much 95% of the population is tired right now, or at least more tired than they want to be.

Ari:
Right. So, the gist of it is, it depends on what we're talking about, are we talking about meeting the diagnostic criteria for ME/CFS, chronic fatigue syndrome, which is a specific set of diagnostic criteria that includes having certain symptoms, particularly post exertional malaise, which is extreme tiredness and exhaustion, being debilitated after physical exertion for 1, 2, 3 days after, and having that symptoms for six months plus. So, there's meeting that diagnostic criteria, but there's also much lesser states of fatigue that are much more common, people who have energy crashes in the afternoon, people who are just operating chronically at much lower energy levels than they did in their youth. And that is very common.

ME/CFS certainly is not super common, but lesser states of fatigue, more mild or moderate states of fatigue, are very common. And we have lots of surveys that show that upwards of 50% of the population, or depending on which demographic you look at, if you look at older adults, severe chronic fatigue is present in one out of three in adults over the age of 65. Lesser states of fatigue, if you ask people, would you like more energy? Do you have less energy than you had when you were younger? 50 plus percent typically of adults will say yes to those questions.

Dave:
In Head Strong, which is my mitochondrial brain book, I cited research from [Dr. Frank] Shallenberger, who said that 48% of people under age 40 had mitochondrial dysfunction and that virtually everyone over age 40 has it, and they just call it aging. Oh, you're supposed to have weak decision making and weak power plant after that age. I don't accept that. That's not how it works, but that's how we think it

works. So, those numbers line up pretty well. And a lot of people who have this are saying, well, I have enough energy. But I think the natural state for humans is to say, I have more than enough energy, I can handle whatever life brings my way. And if I'm just chilling out and I feel like I've had a busy day and then a bear comes at me, I'm going to get up and I'm going to fight off the bear or run away from it, at least faster than someone else. And then it's good to go, and that's just our normal state. But it's not the normal state for most people.

Ari:
Yes, absolutely. I'll give you another data point that lines up with what you just said in an interesting way. There are a number of studies that have taken muscle biopsies of adults at different ages and analyzed their mitochondrial capacity. And they can do this in a number of different ways, measuring certain compounds in the mitochondrial level, but mostly just actually physically counting the number of mitochondria per cell and the total mitochondrial mass per cell. And what they find is, in general, between the ages of 20 to 40, most people lose about half of their mitochondrial capacity, between the ages of 40 to 70, it gets cut in half again. And it can also be quantified roughly by saying, most people lose about 10% of their mitochondrial capacity with each decade of life. Now, one conclusion from that might be, wow, that really sucks that aging does that to us.

But there's also an interesting finding when they look at 70 year olds who are lifelong athletes, exercisers. They take muscle biopsies from them and they look at their mitochondrial capacity and they find that they have the same mitochondrial capacity as a young person. So, what that means is that, this loss of mitochondrial capacity is not just a natural byproduct of the aging process, it is actually the result of loss of hormetic stress in our life. In the same way that if you break an arm or a leg, if you've ever done that, or if you've known someone who has, you get that cast cut off six or eight weeks later and you look down at your arm or your leg, and it's half the size of the other one. And that's because in the span of just a couple months, those muscles basically detected that they weren't needed for survival.

And the body is pretty ruthless in getting rid of any energetically costly tissue that isn't needed for survival. So, it basically says, oh, we don't need those muscles anymore, let's get rid of them. And in just a couple months, they're reduced to half the size. So, at the cellular level, at the mitochondria level, that same process is happening. If you are not challenging and stimulating your mitochondria through hormetic stress, the body basically causes them to atrophy, it gets rid of them and we lose that mitochondrial capacity as we get older. So, I think this to me is one of the most underappreciated aspects and one of the biggest contributors to chronic fatigue, is the loss of mitochondria due to mitochondrial atrophy, not just mitochondrial dysfunction, but the actual decrease of the number and size of the mitochondria in your cells as a result of the modern non hormetic lifestyle.

Dave:
Well, in chronic fatigue syndrome, you are dealing with cells that are poisoned. The No. 1 cause of CFS is toxic mold, and there are other causes, like secondary Lyme disease to toxic mold and heavy metals, or other types of lipophilic toxins. So, let's assume that we're dealing with a population that doesn't have those poisons affecting their mitochondrial function, you still have this, oh, I didn't exercise or didn't do it, I'll just say, do whatever it takes to get enough mitochondrial function that then you can do the work. Because if you're at that level, you're not going to do something on top of the basic necessities for life,

because that's what nature wants, is what you're saying. If it goes away, you don't have enough energy, it's hard to get it back. And so, I just want to call that out. It's okay to do a hack which lets you then do more foundational work, because if you're too tired to improve yourself, you're not going to improve yourself, right?

Ari:
Yeah, absolutely. I totally agree with you. I'll say a couple things on this. What you just said about being too tired to do the work on yourself is huge for people with severe chronic fatigue, especially. People who don't have the drive and the energy to go really overhaul their diet or start a workout program or really do any sort of lifestyle intervention that requires a lot of hard work and discipline. Supplements can be hugely beneficial in that regard. I mean, that there are certain supplements that have been shown in people with stress related fatigue and exhaustion to cut their levels of fatigue, to cut their levels of depression and anxiety and brain fog in half in a week or a month.

Dave:
What's your favorite supplement ingredient that does that?

Ari:
Rhodiola rosea, I would say, is the one that I'm referring to that's been shown to do that in one week. I mean, it's actually pretty mind blowing, to the point where I'm skeptical of some of these studies, where I'm like, whoa, that's a big effect for just seven days.

Dave:
I've been on it for 20 years. Rhodiola is a powerful one. I look at PQQ as a really powerful one as well, even coenzyme Q10 for a lot of people is a big deal, so is acetyl-acetate, which is a mitochondrial metabolite that actually primes the pump. So, there's all these different mitochondrial things you can do, and you're like, oh I have 20% more energy than I did before, maybe I'll go for a walk around the block. And it's not that you didn't want to go for a walk, it's not that you weren't willing to, it's that literally, at the end of the day if I do that, I can't go to work tomorrow. And people don't get it, but it's that big of a deal. And it's not because they're lazy, it's because the battery's dead. And if your Tesla has no charge, it doesn't matter, you can get out and push it. That's your only option. And that's what these people are doing, right?

Ari:
Yeah, absolutely. I'll mention something else. You made me think of a conversation I was having with a friend of mine, who's one of the most, I think, he's widely regarded as one of the world's top peptide experts. You may know him because I know you've dabbled a lot in that world, his name's Jean-Francois Tremblay, and he has a lab up in Canada where they synthesize peptides and he's been on the leading edge of it for a long time. But I was talking to him about MOTS-c, a mitochondrial peptide, and chronic fatigue and if he's had any experience of working with clients who have severe chronic fatigue, chronic fatigue syndrome, or talking to clinicians who have used it. And he had an interesting perspective on it, because it was like, yes, absolutely, it's amazing.

You can get unbelievable results with people with chronic fatigue syndrome, but you really have to be careful not to overuse it, to use it too much for too long. Because if you're, in his words, "Revving up the engine of your mitochondria, you don't want to be pushing that lever all the time because it can result in negative effects." Now, I don't know, I don't have that clinical experience that he's talking about with that particular peptide, but I thought it was an interesting perspective that feeds into this discussion of hacking fatigue in that way.

Dave:
It, I think, really does. I've tried MOTS-c, I couldn't feel anything from it, but I don't have anything near chronic fatigue anymore, I have abundant energy, that still makes me surprised because this wasn't my natural state. So, maybe that's just because I didn't need it. There are though other things that happen. For instance, if you're dealing with toxicities, when I lost the first 50 of the 100 pounds that I lost, well, all of the toxins in that fat get released, and fat stores toxins, toxins down regulate and poison mitochondria. So, I ended up writing a post towards the beginning of my blog and it's still up and it's called Rapid Fat Loss Protocol, how to lose weight faster than you should.

And the big warning is, look, you might fit in your wedding dress, but you're going to feel like crap. So, you have to take all these detox things while you lose weight. One guy did lose a pound a day for 75 days straight, and it's just like, that's dangerous. And so, if you up regulate your mitochondrial function when there's a bunch of crap floating around, you can force them to burn dirty fuel, basically. And it's not going to end well. So, you still have to then start doing the detoxing and other things to get the system back online. At least that's been my experience. Does that match yours?

Ari:
Yeah. Well, you said something at the beginning of this podcast that is very central to my paradigm of understanding energy. And I'll briefly explain that and then I'll tie it back into what you just said. In fact, I've done many interviews where I've talked about it and I've heard this in a number of occasions where people will say, Dave Asprey has talked about this same thing, and you're the only one that I've ever heard that about, you're the only other one that's talking about this, and you alluded to it at the beginning of this podcast.

Basically, in high school and college biology courses, we're often taught about mitochondria as these mindless energy generators, they just take in carbs and fats, pump out cellular energy in the form of ATP. And in recent years, in the last decade especially, it's really been discovered, largely due to the work of Dr. Robert Naviaux, who runs a lab for mitochondrial medicine in the University of California, San Diego, that mitochondria have a second role, and the second role is as environmental sensors. They're essentially the canaries in the coal mine, so they're not just these mindless energy generators, they are actually our energy regulators.

They're deciding whether or not we ourselves should be in energy mode or if they should be in defense mode. And to the extent, they are sensing the presence of various threats or dangers or stressors, they are designed to respond to that by turning down energy production and shifting resources towards cellular defense. Okay. So, think of it like, if you were living in some crazy inner city, I don't know, let's say in the Ukraine right now, and there was an attack in the street, the Russians are attacking and they've got poison gas outside your home in the streets. It would be a terrible mistake to

go, well, let's just keep all the windows open and let the fresh air in and let's go outside and go for a walk as we normally do every day at this time.

The right response when you're under attack is to seal the windows, seal the doors, stay inside, lock yourself in. And that's basically what our cells do when they're under attack, they shift out of energy mode and shift towards defense mode. Your energy levels, I argue, are basically a reflection of the degree to which your mitochondria are sensing that they're under attack and are shifting themselves out of energy mode. So, to the point that you were just making, what would be the consequences of forcing your mitochondria into energy mode when they are actually under attack? And they're designed evolutionarily to be shutting down energy production and shifting into defense mode to, let's say, protect against that mold toxin and or protect against, during rapid weight loss, against all the release of all these stored endocrine disrupting mitochondrial poisoning, DDT and pesticide residues, and all this other crap that's lodged into our adipose tissue that's now being released.

They want to shut down to shield themselves from exposure to that, but now you're forcing them to stay on. In my view, I'm all for hacking when we can do it, I think, in an intelligent way that works with the body. But I think we need to be cautious around making sure we understand physiology accurately and making sure that we're working with the intelligence of our body and not against it.

Dave:
There's a risk/reward for everything you do. Going for that exercise, you might get hit by a car. So, is it worth it? You get on an airplane, it might crash. Is it worth it? Well, yeah. Because I'm going to argue that our mitochondria form a distributed intelligence, and there's really good research for this from Candace Pert. And some of this is, there isn't research, but I can tell you, I can put all the pieces together. So, I think most of our egoic behaviors are actually driven by mitochondrial decision making. That's not even your brain, it's a separate consciousness in your body that's really fast and really dumb. And a lot of this comes from 40 years in the neuroscience company. That's weird, the body felt a stress response in the small window before the brain even gets a signal, so if stress hormones got released before your brain got a signal, and long before you could do anything with a signal, like make a decision. Well, it wasn't you who turned on the stress response, it was them.

And that's our angle for hacking is, and this is what you write about in your book and what is in the definition of bio hacking, is change the environment around you and inside of you so you have full control of your biology. No. 1 thing you want is energy, because it turns off fatigue. But the other thing I want to ask you about is, I believe that somewhere from 50% to 70% of anxiety that people are feeling is not mental anxiety, it's actually biological anxiety from the mitochondria going, we're under attack. So you feel this sense of doom or this sense of irritation, and then you blame CNN, well, actually they deserve the blame, or you blame your mother-in-law, or you pick a target and then your brain makes up a story. Because it knows that the stress is there, there must be a reason, but the brain can't see the mitochondria because they're faster than the brain. So there's all this weird stuff going on. So, what's the relationship between fatigue and anxiety, in your experience?

Ari:
Yeah. I mean, I don't know if I would go as far as where you just took it. I'm not saying that I think you're wrong, I'm sure that there's something to what you're saying, but I don't know that I've seen research to

really, I don't know, make me go to that level. I think what you said is a very interesting hypothesis though. I'm fascinated with this field of research called mitochondrial psychobiology.

Dave:
There you go.

Ari:
And there I've interviewed a guy who's one of the primary researchers in that field named Martin Picard, who works with Doug Wallace, who's this legendary mitochondrial researcher.

Dave:
Yep.

Ari:
And they've performed some really interesting experiments. They did one study where they had people basically go on stage and have to give a speech, public speaking. And as you probably know, I think they say that people have more fear of public speaking than they do of death, so it's a pretty intense thing for most people. And then they basically had them give this little speech and then they had an audience attack them personally, so just shout insults at them. And so, for most people, it's a pretty extreme stress. And they showed, actually, the leakage of mitochondrial DNA in the bloodstream within a matter of seconds of this extreme stress. We also know from lots and lots of other studies that, there's studies on depression, there's studies on anxiety, there's studies on several other mental health and psychiatric disorders, that mitochondrial dysfunction is associated with that. So, there does seem to be a very strong bidirectional link, the function of your mitochondria impact upon your brain function, your mental health, your mood, your cognitive function, and vice versa. Extreme emotional reactions and stress reactions directly impact on your mitochondria within seconds to minutes.

Dave:
You can be tweaked in ahead and hurt your biology or can be tweaked in your biology and hurt your head. We train that network to determine what is a threat and what isn't, because it has to be able to react to threats before we can. That's the convenient part of you that jumps when a tiger comes out of the tree before you decide to jump. And so, there's all this neat psychobiology and stuff we haven't figured out. But the idea you that your mental state is one of the many variables that affects mitochondria is really important. But do people get chronic fatigue because they had a bad breakup?

Ari:
I think that's possible, actually.

Dave:
It's possible, but rare, right? And usually, there's other things that weakened the system to a certain point, they didn't have the resilience to handle that. And resilience just basically means you can handle a

stressor and then return to baseline quickly and effectively. And when you handle a stressor and it keeps you stressed for a long period of time, and then your system degrades, you didn't have resilience.

Ari:
Resilience is something that we've often, most people, conceptualize as a psychological phenomenon. And there's certainly a psychological aspect to it, a mental toughness aspect to it. And just life experience, what you've dealt with, allows you to become more resilient to those kinds of experiences. But there's a physiological basis of it as well that revolves around mitochondria that, I think, is not well understood, but is incredibly important. And it relates back to what I was describing before, with mitochondrial capacity, the loss of mitochondrial capacity, as you lose mitochondria, you basically become less resilient in the face of these stressors. So, the mitochondria have this role as environmental sensors, they're not only sensing the presence of various stressors, but they're actually tasked with, to some extent, directly fighting them off or defending the cell against those stressors or coordinating a response to it.

So, this is true, whether it's a pathogen, it's true whether a virus or a bacterial infection, it's true whether it's psychological distress, it's true whether it's environmental toxicants, it's true whether it's sleep deprivation, poor nutrition, all of those things, the mitochondria are being tasked with fighting against that source of stress at the cellular level. And basically it's like, imagine that we were together right now in the same room and that we look over to our right and oh, there's a building on fire, and now we have to go take buckets of water and try to put out that fire. Well, is it easier for just you and I to do that, just the two of us? Or would it be easier if everybody watching this live right now, in the whatever hundreds or thousands of people, were also taking buckets of water and helping us? Or even if we just had, let's say 20 other guys, in addition to us, it would be way easier.

So, what I'm getting at is, the more mitochondria you have in your cells, having youthful levels of mitochondria, lots of big strong mitochondria filling your cells versus what's common in older age of losing 50%, 75% of your mitochondria, you have lowered your resilience threshold. You have lowered your mitochondria's capacity to deal with that stressor and then return the body to health and homeostasis and high energy levels. In other words, the mitochondria have a certain limit of what level of stressor they're able to tolerate and maintain health and high energy levels. And if you exceed that limit, then you get fatigue and you get other symptoms, and ultimately, various kinds of diseases. So, the more mitochondria you have, the bigger, stronger your mitochondrial networks are, the higher your resilience threshold, the higher your capacity to tolerate various kinds of stressors. And that is the physiological basis of resilience.

Dave:
I love that definition. And there's an emotional one as well, because if you handle it physiologically and then emotionally you lose your mind, then your mitochondria also take a hit. I look at it as, you want to have a big army with lots of troops and you want the troops to be very healthy and strong, they should be good fighters. You also want them to be obedient troops, and that when the general, which is you, or the sub generals and the commanders and all, which is actually not your decision making, but these are other higher-level systems in the body, like liver regulation for all the mitochondria in the liver, for instance, they also need to listen to those. So, you can have command lines that are screwed up that'll

cause poor mitochondrial function, because they aren't well organized, or you can just have weak ones or you can have not enough of them. And those are all hackable things to do. You've listed six major causes of mitochondrial dysfunction in your book, can you go through all six from memory?

Ari:
Yeah. So, I mean, these are six nutritional causes specifically. So, circadian rhythm disruption, blood sugar dysregulation, poor body composition, poor gut health and poor brain health.

Dave:
And neurotransmitter and hormone imbalances, I think, is your poor brain health.

Ari:
Yes. Yep.

Dave:
And did you say microbiome in there?

Ari:
Yeah. Gut health.

Dave:
You did. Okay. Good gut health. There you go. All right. So, that's a good list. And guys, if you want it one more time, circadian rhythm, too much body fat, gut health, blood sugar, nutritional toxicities or deficiencies, and neurotransmitter/hormone imbalance. That's a fantastic list. Problem is, if you're listening to the show going, I'm tired, now I'm already overwhelmed, my mitochondria just got another hit because I'm feeling overwhelmed, how the hell would you know where to start?

Ari:
Start with the low hanging fruit, start with the easy, simple stuff.

Dave:
Yes.

Ari:
Here's the thing, I think that a lot of who are brought up in the west, in the United States, in North America, who are brought up in a conventional medical paradigm, the United States and New Zealand are the only two countries in the world that allowed direct to consumer advertising for pharmaceutical companies. And I grew up in the states, I was seeing pharmaceutical ads on TV from the time I was a little kid, being bombarded with them. And it's so easy when you have that influence to start thinking from a paradigm of, every one specific problem, physiological problem, health problem, requires some very specific targeted biochemical intervention that's unique for that specific disease state. So, what's the drug I take for Alzheimer's? And what's the drug I take for depression? What's the drug I take for my

high cholesterol? And the drug I take for this and the drug I take for that. We all start thinking in that paradigm when we're brought up in the west. But when you study physiology at a deep level for a long time, as you and I have, you start to realize everything in the body is interconnected. And so-

Dave:
Hold on, hold on. We're going to have to ban this episode. You're now offending the authorities at the drug companies. You just can't say that. American Medical Association is angry right now, how can you be a kidney specialist? I mean, come on.

Ari:
Well, I didn't mention the V word, so I think we're still okay.

Dave:
That was the sex episode, that's a different one.

Ari:
Oh yeah. Sorry.

Dave:
Oh, the other V word. Sorry, sorry. I get all confused. Now we'll definitely get banned.

Ari:
Yes, definitely. So, as an example, just to look at circadian rhythm, okay, circadian rhythm, and I won't... Your audience is sophisticated, I'm sure you've talked about this a bit, so I won't go into a whole bunch of the physiology. But we start to look at these biological clocks, the central clock in the brain, the peripheral clocks throughout the body, and initially it's thought, oh, the circadian rhythm, it's really important for our sleep and wake cycles. Well, then as you start to dig in deeper you start to discover, oh, circadian rhythm also impacts on many different neurotransmitters from dopamine to serotonin, to GABA, to orexin. It's impacting on different biochemical processes at the mitochondria level, it's impacting on the lymphatic system, this process of cleaning out toxins from our brain every night, it's impacting on many different hormones that impacts so many aspects of our mood, our energy, our libido, from thyroid hormone, to cortisol, to testosterone, to growth hormone, to melatonin.

And then you just look at the melatonin story, many people think of melatonin, oh yeah, that's a sleep supplement, melatonin. And they don't even realize, melatonin is a hormone produced in our body. And the other part of the story, there's many layers to this, but melatonin is actually, turns out, is basically the most important mitochondrial antioxidant and is vital for protecting our mitochondria and our neurons, and has profound anti-cancer effects as well, super important for preventing the development of cancer. So, you start to realize, and then this other, well, actually I won't go there yet. You start to realize that this one lever of circadian rhythm is actually impacting everything, it's impacting everything from brain health to mitochondrial health, to gut health, to immune health, to body composition, to levels of inflammation, to insulin sensitivity, to libido and mood. And so, again, just to loop things back, we need to get out of this mindset of, oh, I have this specific problem, and that

problem is caused by this specific biochemical abnormality, and therefore I need this specific drug to affect that pathway. And we need to start understanding how to work with the systems of our body, to pull different levers, to optimize the entire system, to have beneficial impacts on our physiological function as a whole.

Dave:
You said something again there that a lot of people don't know about, it's that melatonin causes insulin resistance. So, if you were to take melatonin with an ice cream cone, your blood sugar is going to go higher. If you eat after the sun goes down, you will not handle that food the same way. And this is the biggest reason that I tell people, look, just don't eat after the sun goes down, that midnight snack is truly harmful. And maybe if you had only fat for a midnight snack, or maybe a little bit of protein that doesn't raise your insulin and you needed that in order to sleep, okay, fine. But the typical way we're eating, we're eating at the time when it causes diabetes like symptoms, and just shifting that can have systemic effects. And that's just one of the things that melatonin does. Well, let me ask you this, do you take melatonin?

Ari:
Such a complex answer. So, I've discovered something that isn't talked about widely, but certain people seem, and it seems to be genetic because both me and my father have it, seem to be hypersensitive to melatonin. If I take a three milligram, which is a typical supplemental dose of melatonin, it actually causes insomnia for me. I sleep terribly because of it, and I will wake up the next morning really groggy and feeling pretty awful. And I've tried it many times because I've been so impressed with the research on melatonin. What I found is that I can take baby doses of it, I can take very small doses. Actually, a physiological dose is about 300 micrograms, which is-

Dave:
0.3, right?

Ari:
0.3 milligrams, yeah. And there's a company called Herbatonin, which makes a plant-based melatonin. I don't know why this affects me differently, but even if I take the same dose from another kind of melatonin, I'm much more sensitive to it, but the Herbatonin seems to work well with my body. I'm not-

Dave:
Maybe because it's plant-based it just doesn't work very well at all, so it doesn't cause that effect.

Ari:
It definitely does cause an effect though. Your theory is, honestly, legitimate, that's possible. But it does have an effect, for sure.

Dave:
Okay.

Ari:
But it's a subtle effect. So, I don't have a strong answer on that. The research on supplemental melatonin is, I would say, overwhelmingly positive and it's been used in lots of different disease context, neurodegenerative disease, bowel diseases, cancers, with pretty remarkable results, I would say in most cases. So, I almost have an attitude of, I would like to supplement melatonin because I'm so impressed with the research, but it just doesn't work with my physiology.

Dave:
And I used to take the biological dose, 0.3 milligrams, and I think that's safe for the vast majority of people. And most supplements have 10 times that dose, but there's also absorption and timing and things, so three milligrams works. And then there are a few people out there who are taking 20, 30, 40 milligrams because of positive effects on repairing the pineal gland and other things, which seems a little bit high. So, I tested myself, I took 20 milligrams for six months and it probably improved my sleep. In fact, it quantifiably did, to a certain extent. But I backed off to 10 milligrams of time release, which is what I take now when I go to bed, and I get the best night's sleep when I do that. And I think there's anti-aging effects from having higher than physiological amounts of melatonin during sleep. Then again, I sleep six and a half hours a night and I wake up by myself after that.

And I'm, oh, that's weird, I got two hours of deep and two hours of REM, I actually think I just recovered well last night and I'm done sleeping. It's different if you wanted to sleep more but you couldn't. So, I didn't used to be like that.

Ari:
No.

Dave:
But I like waking up that way. And I think my dose works for me. And guys, I'm 6'4 and I have a history of neurological inflammation, for my entire life, and autoimmunity and things, so that might be too much for you. But there's a case for trying a higher dose, but don't take it with dessert, because it's going to mess you up.

Ari:
Yeah. I will say one more thing on this, I have heard, I don't know if you've had Dr. Ben Lynch on your podcast, he's a buddy of mine and-

Dave:
Absolutely.

Ari:
I've talked to him about using high dose melatonin and he's, I've seen him warn against it on a number of occasions, he's concerned with actually too much of this antioxidant leading actually to pro-oxidant effects. And I've also heard people suggest negative effects in women on estrogen, metabolism, and

things like that. So, I do have a little bit of caution with recommending super high dosages, but I think 10 milligrams is pretty moderate compared to some of the research I've seen, 40, 60, 80 milligrams a day.

Dave:
And that would be for a short period to repair some system, I don't think people are advocating for taking that every day.

Ari:
Yeah.

Dave:
And the point about increasing oxidation, even if you do something like vitamin C and you take 50 milligrams a day or 25, like Linus Pauling, who had two Nobel prizes and took, I believe, 25 milligram... Sorry, 25 grams a day, that's 25 large vitamin C pills a day, lived till he was 90. It does suppress mitochondrial function, even Metformin, the drug that some people in anti-aging are big fans of, certainly something I've experimented with, it reduces mitochondrial function. So, mitochondria need to make oxidative molecules, and it's a signaling molecule. It's why ozone therapy works. So, if you're always taking high dose antioxidants, your exercise doesn't create benefits and your mitochondria actually can't send a signal to other mitochondria that says, hey, let's build more, let's be strong.

Ari:
Yeah.

Dave:
So, there's a case for them and there's a case against them. But too much antioxidants all the time, no. No antioxidants ever, no. How would we know how much to take? What do you do to look at that?

Ari:
Yeah, it's a great question. I love what you just, there's a lot I want to say in response to it. I want to comment one more bit about melatonin that's interesting because there's a somewhat new discovery around it. So, I mentioned melatonin is this incredibly important antioxidant at the mitochondrial level, well, it's turning out there's a number of lines of research that are now suggesting that mitochondria actually produce their own melatonin-

Dave:
A hundred percent.

Ari:
At the cellular level. So, we need to get out of this paradigm that all the melatonin is coming from the pineal gland, going into our bloodstream and then ending up in our mitochondria. It's actually been shown in, I think, in animal studies where they take out the pineal gland, that it doesn't change the concentrations of melatonin at the mitochondrial level. So, the other aspect of this, this is super cool,

particularly you've been into red light for a long time, as I have, and I've written a book on it. This is such new information, it didn't even make it into my book a few years ago. I'm going to update that shortly. But there's research now suggesting that red and infrared light directly impact upon the production of non-pineal melatonin, melatonin at the mitochondria level, at the cellular level. So, it seems that light exposure is actually one of the big keys to our mitochondria producing this incredibly important endogenous antioxidant. Melatonin also impacts on other endogenous antioxidants, glutathione, catalase, superoxide dismutase.

So, what I think is that it's going to turn out that much more, that maintaining proper redox balance and preventing oxidative stress and oxidative damage, which is one of the main drivers of aging and disease, is much more about supporting and optimizing and endogenous antioxidant production than it is about using supplemental antioxidants. It's not to say that it's black or white and you should never use supplemental antioxidants. But I think that that story, and particularly I think it's going to turn out five years from now, I think everybody's going to start to recognize how important melatonin is to that story of preventing oxidative damage at the cellular level. So, that's one thing I wanted to comment on.

And then the other thing you commented on in passing, which is super interesting, that I want to expand upon a bit, is that we used to have this paradigm that free radicals are bad, antioxidants are good, we need to squash all the free radicals because they're driving disease. And it used to be thought for many, many years, for decades, that these free radicals are causing this oxidative stress and causing aging, we had a free radical theory of aging. And so, as an extension of that, we would expect that by using, like Linus Pauling did, so much exogenous antioxidants, that it should slow down the aging process, except we know from lots of research that that's not true. We also know from lots of research that things which actually cause the production of lots of reactive oxygen species, free radicals, like exercise, for example, or most other types of hormetic stressors-

Dave:
Or saunas, or ozone, or cold therapy, all the stuff that we do, right?

Ari:
Right. So, paradoxically, they actually extend lifespan, rather than shorten it. So, what's going on there? Then what's interesting and one of the big breakthroughs, which you alluded to in passing, is a decade or two ago, maybe 15, 10, 15 years ago, a number of researchers basically said, well, we know exercise is really beneficial, it has all these amazing effects, it's associated with longer lifespans, prevents all kinds of different diseases, but the problem with it is that it produces all these damaging free radicals. So, what if we take supplemental vitamin C, vitamin E, vitamin A before or after exercise to minimize that? And they did those studies and what they found in those studies is that it is it negated, it canceled out most of the benefits of the exercise.

Dave:
Even vitamin A? I don't think A is particularly antioxidant, that was mostly vitamin E, right?

Ari:

They've definitely used vitamin A in some of those studies.

Dave:
Interesting.

Ari:
I don't know if they've only used vitamin A, it might have been a cocktail with vitamin E, vitamin C. So, I don't know to what extent you can attribute the effect directly to vitamin A.

Dave:
Because A is typically not antioxidant, it's more like mineral absorption. It is a circadian vitamin, but if you take it in relation to vitamin D, it seems to not negatively affect mitochondria probably positively.

Ari:
Yeah.

Dave:
That's part of my next book, I have some stuff in there about the fat solubles. There's some really neat stuff you talked about there, but one thing I just want to talk about, you know about red light, I know about red light, and there are so many companies doing, like 1980s blue blockers and saying that that's what you do for sleep. I have written the patent for TrueDark, my circadian biology company, and there's four colors of light that affect your timing system. And blue light is just one of the four colors, and blue light affects melatonin level. So, if you block blue, your melatonin will go up, but your timing system will still be broken, which is not a good move. And that's why you see me at night in pictures or the Danger Coffee pictures, whatever, I'm wearing these unusually colored reddish, but with a variation in it, glasses.

Because that's actually covering all five aspects of light and how it talks to your central clock. So, it's just a little bit more complex than that. But I'd say for most people, I think it's a pretty good idea. After the sun goes down, don't eat anymore, and take a melatonin maybe two hours before bed, and just watch your sleep score on whatever sleep tracking you use. I'm a big fan of SleepSpace, which is a free app, but they also have a sensor thing. And man, you just realize I have a very noticeable change in my deep sleep. For me, I doubled my deep sleep. But blue blockers won't do that for me, they don't change my deep sleep number at all. But blocking all four colors does. So, just understand from a mitochondrial perspective, red light is magic, just to look at red light. And the mechanism action for red and infrared on increasing melatonin, I would argue that mitochondria want to make melatonin when there's an absence of other light, but red light makes more electrons available and makes them move more effectively.

Ari:
Red and near-infrared light also have another mechanism of action that's very important, which is retrograde signaling. They are impacting directly on the gene expression from the nucleus. So, they're shutting down NF-κB pro inflammatory pathways, and they're stimulating the expression of genes

involved in growth and regeneration, basically growth factors. So, in muscle tissue, they're stimulating increased IGF-1, in the brain they're stimulating increased nerve growth factor and brain derived neurotrophic factor, in the skin they're stimulating increased collagen production, fibroblast activity. They're basically stimulating whatever specific growth factors in whatever tissues they are in, in the thyroid gland, hormone producing glands and whatever. So, it's possible that along with modulating dozens, maybe hundreds of different genes, to do those kinds of effects, maybe melatonin is paired with that in some way, is involved in those healing and regeneration pathways to reestablish proper redox status. But I don't know, I think your theory is a good one.

Dave:
Do you put red light on your balls?

Ari:
Man, I don't think I've ever been asked that in an interview before. Yeah, of course. Who doesn't?

Dave:
Okay. Corollary follow up question, butthole sunning, yay or nay?

Ari:
So, I'm a fan of naked sunning. I have never done the full, what do you call it, maybe a plow pose where I've attempted to get it in my butthole, but I'm fan of naked sunning.

Dave:
You're missing out, it's just like eating Mexican food. I mean, just don't get sunburn is all I'm saying. Okay guys, in reality, I did that once for a picture and it got picked up in the press and it was a humor post because, no, I don't think you need to tan your taint. But there is evidence for sunlight on your testes and red light on your testes. One of the reasons is probably mitochondrial efficiency, we talked about. The other one though, is that red light increases nitric oxide. So, if you put one of the TrueLight energy panels with the infrared and red over your groin before you go to sleep, wake up in the morning and look at the quality of your kickstand, because nitric oxide is a real thing that changes blood flow. So, I see a difference from that for sure.

Ari:
There's actually a study where they have looked at men who have erectile dysfunction, who have difficulty getting erections, and they actually found an association, a strong association with... Oh geez, I'm forgetting the specific condition. But basically, a deviated septum or something to that effect, where they have difficulty breathing through their nose. And they found that as a result of doing surgery to correct that, so that now that they can engage in nasal breathing, the erection performance, I guess you would say, increased dramatically as a result of nasal breathing, which we know is one of the big keys to producing nitric oxide in the bloodstream, as opposed to mouth breathing. So yeah, to your point, there is a powerful relationship with nitric oxide and red and near-infrared light, and sunlight also, UV light also impact on that.

Dave:
Mitochondria are exquisitely sensitive to UV light and they need some of it, but not too much. It seems like it's a stimulating molecule, oh, maybe I should make some antioxidants to protect myself from radiation. Which is another reason that I tell people, get some sun, but maybe not too much.

Ari:
Yeah. I'm a huge advocate of sun exposure. The challenge with it is that genetics of skin type make a massive difference in what is the appropriate dose for the individual. It can vary between, maybe your optimal dose is five to 10 minutes per day, or maybe it's three to five hours per day. I'm definitely, I have a lot of Mediterranean and North African ancestry in me, and I'm definitely more on the side of the spectrum where my body does best with more sun exposure. And my health really suffers if I'm in a place where I can't get much sun exposure.

Dave:
I'm the same way. In fact, the DNA company looked at my vitamin D receptor genes and they said, "We've got bad news for you, Dave, based on your vitamin D receptor genes and the rate you use vitamin D, you should be living on a tropical island. Based on the fact that you are white, sadly, that's probably not going to work for you either." So, I'm damned if you do, damned if I don't. I need to get enough sun to be happy, but not enough sun to cook my frail white skin. So, I don't know how to solve that problem, if you come up with it. Right now, what I do is I inject melanotan, which is a hormone that stimulates the formation of melanin. So, I can get a tan in very little time, and the tan naturally protects me from the sun.

Ari:
Yeah. And isn't, if I remember correctly, I've never used it, but if I remember correctly, melanotan also impacts on libido and erections as well.

Dave:
It has a side molecule that you can buy separately called PT-141. And if you want to feel like you are in 11th grade again, you inject that stuff. And if it doesn't cause nausea for you like it does for some people, you're like, could I not inject that again? Because this is too distracting. It is a very strong... Much stronger than Viagra or something like that, if that works for you.

Ari:
Yeah.

Dave:
So, it does have that side effect, you have to do low doses unless you just want to be terribly distracted it all the time.

Ari:

Yeah.

Dave:
So, there's that. There's something else though, and the reason I mentioned that is not that I'm just single minded, I didn't inject it this morning, it's that melanin is actually electrically active. And this is something very few people talk about in the context of mitochondria. So, if you look at mitochondria as power generators, as one of their many functions, what melanin is, is like a Tesla power wall, so it actually stores a small amount of energy, like a capacitor would if you're an electrical engineer, and it can release it. And this is why, the darker your skin tone, the less your skin ages. It's one of the many reasons, not just UV protection. And it's also why we have melanin, this dark compound in the back of our eyes where you need sudden bursts of electro activity. And we have junk melanin in the brain, which anytime scientists say something is junk, what they mean is, we haven't studied it, yes, and we're arrogant.

Ari:
Yeah. The appendix is just a remnant of evolution, you don't need that, just pull that thing right out.

Dave:
Exactly. Right. Yeah. It couldn't have a function, let's just get rid of it. Just like a foreskin, just cut that thing off. Who needs it, right? Well, maybe it was there for a reason, just saying. So, I actually found a couple scientists who spent many years in Mexico looking at this, why is there melanin in the brain, in the back of the eye where there's no sun? And the answer is, it can create electrical signaling when needed. So, it's basically there as a backup power plant. So, bottom line is, a healthy tan actually is healthy, as long as you didn't stay in the sun for long you got skin cancer from it if your skin is pale.

Ari:
And there's advantages to building up that natural, innate sunscreen that we're all born with the capacity to produce. Well, almost all, unless you're extreme Fitzpatrick type 1, or you have albinism or something like that.

Dave:
Exactly. Now in your book, you go through all six of those things that we talked about, the main causes for mitochondrial dysfunction. And you look at ways that you can go in and you can do something about them. And I want to highlight, if you guys decide to read Ari's book, you don't have to do everything, it's Ari's job, it's my job to show you the universe of what you can do, to explain why it's important and why it's worth your time and attention. And just pick one and do it, and if it works, which it probably will, you'll get some amount of energy back. Maybe it's 5%, maybe it's 50%, but that energy, you could say, I'm done, or you put that energy into doing the next thing. And then now you have 20% more energy, you're like, oh, you know what? I can actually put my glasses on before I go to sleep, I can get blackout curtains, I can eat dinner earlier, I can do whatever, I can take a supplement.

This was my path. Of course, it cost me a million bucks and took a long time because there was no roadmap for this stuff. It was my path to getting to where I am now, where like, wow, I like how I

feel. And you have a list of supplements in the book, seven supplements, all of them I would agree with. Things like methylated B, vitamins, and astaxanthin, which is something I take an enormous amount of every day and-

Ari:
Which, by the way, just a side note, also builds up in the skin and acts as an internal sunscreen.

Dave:
You nailed it. It's one of the reasons I take it, is I don't get sunburned very easily because I take a lot of it. It's also eye protective. And when you take enough astaxanthin, it actually can become incorporated into the mitochondrial membrane where it can conduct electrons much better than other things. So, if you dope your mitochondria with this, you get supercharged mitochondria, but you have to take probably 20 milligrams a day. And I would say, take it with a fatty substance, maybe emulsified in Danger Coffee, so butter, some crazy idea like that. So, astaxanthin, A-S-T-A-X-A-N-T-H-I-N, is that specific thing.

And you've got a great, really, chapter on supplements, which is really cool. And so, I would say this is a great comprehensive look at, what do you do for mitochondria? And if you've listened this far, it's just worth your time to know this stuff, you're not going to take all the supplements. Except I'm pretty sure I'm looking through the list from my notes, there aren't any of them that I don't either take sometimes or all the time. So, it's a good list. Like CBD oil, I take it sometimes, don't take it sometimes. I do notice the difference in sleep from some forms, not others. That's on your list. But overall-

Ari:
If I ask Dave Asprey, what supplements you take? You'd be like, all of them. You take everything

Dave:
Right. Let me pull up my dump truck that has the ones I'm taking today. And the reason I do that is, from what I've learned over the years, I'm planning to live to at least 180, I'm willing to take something that is likely effective based on four studies that are strong studies. And every study says at the end, more research is needed, which is the way researchers say please fund my next year of eating. It doesn't mean more research is needed, because every paper that comes out helps us to tighten the direction. I'm heading north, okay, if I'm heading north, maybe I wanted to go three degrees left, three degrees right, but at least now I know I'm headed north. So, this is how you use it as a functional human being versus an academic, where I need a hundred percent certainty. I promise every academic out there, you're all wrong

A hundred percent. 200 years from now, we're all going to be face-palming going, can you believe that they didn't know that the universe was holographic and quantum, and that we're actually all controlled by video game characters? I have no idea. But there's stuff we don't know. It's just, are we certain enough that if we do this, we're good to get this, if so, I'm going to do it. And so, my rationale is not that everyone should take a hundred plus supplements a day, it's that I'm doing it based on my biology and my goals that are not normal. So, good job on a great supplement list in the book.

Ari:
Thank you.

Dave:
All right. Thank you for being on the show. Your new book is called, Eat For Energy, and you'll find it at theenergyblueprint.com. And there's just a lot of knowledge here. And I think we made a pretty convincing case that if you don't have an army of mitochondria that is both numerous and individually powerful, you're doing it wrong.

Ari:
Most definitely.

Dave:
To our live audience from The Upgrade Collective, thank you for your participation and for all of your help with me crowdsourcing questions. And I appreciate your time as well. Guys, if you'd like to be in the live audience and be able to participate like that, go to ourupgradecollective.com. I will see you all in the next episode. You are listening to The Human Upgrade with Dave Asprey.