

How To Know If You Have Poor Mitochondrial Health And The Best Way To Fix It

Ari Whitten, MS
with **Datis Kharrazian, PhD**



Ari Whitten, MS

So welcome, Dr. Kharrazian, and such a pleasure to have you. Thank you so much for joining us.

Datis Kharrazian, PhD

Thank you very much. How have you been?

Ari Whitten, MS

Okay. So first of all and there is a lot of talk of mitochondria these days and we have had 10, 20 years now of research that has really brought to the forefront the importance of mitochondria for a long time, this is one of many organelles in the cell. It is the powerhouse of the cell, quote unquote. And, it takes in carbs and fats and pumps out ATP. And that is all you need to know about those little mitochondria in your cells. And now we have had a couple of decades of research that have put mitochondria at the forefront of discussions around health and many different diseases. So there are also, I would say, different stories, different narratives, and paradigms that have been presented around mitochondrial health. I'm curious just to start this. How do you see mitochondria in the overall picture of human health and disease and longevity? How would you describe their role?

Datis Kharrazian, PhD

Yes, a good question. So ultimately, if you look at the studies on longevity, the key thing that they find in centenarians and people that are living healthy lifespans without chronic illness is that they have resiliency. And resiliency could be like temperature resiliency, they could be immune resiliency, blood sugar resiliency, cognitive resiliency, physical exercise resiliency. And resiliency can easily translate to how effective the mitochondria are in the systems. And even if the mitochondria get focused in as the energy powerhouse of the cell and it makes energy but is a cell signaling unit. I mean the mitochondria does trigger the initial stress response. The mitochondria does initiate through different proteins normal immune activation for an infection and it generates heme to produce hemoglobin. It is like what we need to recover and in a clinical setting not only longevity mechanisms of aging, but a person's ability to recover is directly related to the fitness of their mitochondrial systems. So if you have three different people say two different people say one person had a traumatic brain injury. One person has a chronic viral

infection. Let us say both people have the same things, like the example to try to manage, if you will, both people, the one that has greater mitochondrial efficiency probably can recover faster. So it is a viral infection that one has probably greater mitochondrial integrity and is going to recover faster. So whatever this condition is in our ability to heal ourselves, homeostasis is all energy dependent. So if you look at so many biochemical pathways, he is all these diagrams and charts like that all run on ATP. And the mitochondria we have are directly impacted by the things we do in our life. So we have to be able to make mitochondria of mitochondria biogenesis. They require activation.

It will clear mitochondria mitophagy and things like lack of sleep or overeating or hormone deficiencies. All these things can impact how we clear out these different hormones, these mitochondrial proteins, and structures. So it is one of those things where as a clinician, the biggest clue for us is they come in and they say they have fatigue, and then we are okay, the mitochondrial system is inefficient. And then the question is, what kind of fatigue do you have? And the next question is what do you do? And ultimately, when we look at mitochondria from a clinical perspective, the mitochondria has needs, the mitochondria have to have glucose and or ketones one of other. But let us just include glucose for now. But if it has glucose and then it can, it is what it needs the substrate to run the process. If someone gets fatigued after meals or gets Chicken Little between meals, you already know a mechanism where the mitochondria can not function. The mitochondria needs oxygen. So if someone has asthma and we hear wheezing and they have some allergies that are respiratory, we know they are going to be inefficient. So is anemia and they can not carry oxygen. The mitochondria, which we know that there is not going to be a chance for recovery.

In a clinical setting, we have like dealbreakers, there is no way they are going to be able to recover because their mitochondria is not able to produce ATP and get those things to work. We know the mitochondria are extremely sensitive to free radicals, and oxidative stress so like chemical loads, they created them to respond to the depletion of antioxidants. Those things will cause the mitochondria to fail. So what we are trying to do in a clinical setting is start to dissect that. What's the cause of fatigue? How many markers would they have that are causing the expression of fatigue? Because fatigue is basically a chemical window of mitochondrial efficiency. So people that have a great mitochondrial function are the ones that are impaired, that recover that can recover quickly from workouts. So we hear things like, I can not focus for a period of time or I can not work out like I used to, I can not recover from my workouts. Those are the clues to us that their mitochondria systems are inefficient and typically it starts with loss of endurance first. So it'll be, I can not run like I used to. And this muscular mitochondrion, I can not read as many chapters as I used to. I can only read like three pages and it's brain mitochondria.

So whatever system we are looking at we will see is mitochondria fails is fatigue is like endurance issues first and then gets into progressive fatigue. And the way I kind of look at my patient population is when they tell me that fatigue is one of the other things that may be actually red flags of what the mitochondria need, that we need to find that interim in fatigue, that they have

fatigued all the time, or is it the debilitating fatigue? In debilitating fatigue, we worry about things like cancer, malignancy, and autoimmunity to the mitochondria, which we see with people that they have, like the so-called chronic fatigue patterns and things like that. But that is kind of the thought process that exists. Kind of rambled on. But you answered a question. I start though.

Ari Whitten, MS

That was great. And I love that you have presented resiliency at the beginning of your answer as a sort of foundational aspect of your answer, because this term resilience is something that is obviously incorporated in, in modern vocabulary, but it is typically framed as, a purely psychological concept, as something that happens in the mind. It is like, how resilient are you? But there is a physiological basis to resilience. And as you said there, it is all about stress buffering capacity at the cellular level. And stress buffering capacity is essentially synonymous with energy production capacity. How much energy can your cells produce to meet the demands that are on them from those stresses which relate to your ability to not only handle the stress but also gave the example of traumatic brain injury or viruses or things like that? How quickly can you bounce back, which is oftentimes the difference between bouncing back or not bouncing back, being stuck in chronic illness, if you have such a degree of overwhelm of your cellular capacity for bouncing back?

Datis Kharrazian, PhD

Absolutely. When you look at a chronic patient, the person who's gone through the health care system and they are getting all these different diagnoses and I can really figure out what's going on. And one from practitioner to the next to the next. The key thing is they do not have the ability to recover whatever it is. Then the question is why do they not have the ability to recover? Then executive pathways. One of the key things is ultimately what's causing the mitochondria to not function, to not work. And it can be a whole list of things. That is where it could be a little confusing. When things go wrong, people will hear about mitochondria function, they get, we need some CoQ10. We have some CoQ10 and we had like really fancy niacinamide and, you know, nutrients like that or pycnogenol or something and everything is going to work. And it is like, no, this clinical setting, we see chronic patients, they are coming in with bags full of supplements. It is not a supplement deficiency issue. For some people taking various pharmaceuticals can give them some minor function and maybe help on the recovery pathway.

But you really have to treat the underlying mechanism of what's happening. So usually when people can not recover, it is this load of various things that are causing the mitochondrial to not function. And then the basic things we already know, we know people need to have sleep, we know people have to have movement. People have to have nutrients and a healthy diet. We know people need to have relationships. All these things actually have a chance to impact mitochondrial function, whether it is Biogenesis or Mitophagy, or these different pathways. Now, ultimately, I see a lot of patients that have traumatic brain injuries they work with. We're trying to help them recover. We will see patients that have chronic illnesses and they can not recover. And

the first question is, can they make mitochondria and how do you get mitochondrial Biogenesis? How do you make more mitochondria? Because we can change our mitochondria concentration in our tissues and cells by things we do. If you look at the literature, what they are looking at is the signaling agents for mitochondria, biogenesis, and for the most part, there really tend to be things like antioxidants as you know things like green tea, things like virtual. They turn on the killer messengers that can and can theoretically produce many contra, but they do not produce mitochondria they just turn on the messenger pathways. And then you actually have to produce many hundreds of activations. So you actually have to stimulate movement and you have to have more misses and stress to the system too, to make those things work. So you know.

Ari Whitten, MS

The analogy that I often use is building muscle. It is like you are not going to build muscle unless you have created the demand that makes your body want to adapt to that demand by building more muscle.

Datis Kharrazian, PhD

Exactly. It is the same thing we would do like neurological rehabilitation if some had a stroke or injury. Then the question is like, what can not you do? I can not walk in a straight line. Perfect. That is your rehab.

Ari Whitten, MS

Exactly.

Datis Kharrazian, PhD

That is my news. What are you going to do? The range of injured now has to reconnect. And mitochondria are necessary so you keep activating those pathways, you are going to stimulate mitochondria biogenesis. So I think one of the key things that is missing in a clinical world, especially in a world of nutrition, is just focusing on top like a supplement dump, like a hormone dump, like cleaning toxins and not really discussing activation and what things are. Back to the scenario, if a person can not read a chapter, they can only be three pages and said, well, the thing is, up, I read three pages, I'm done. No, you are going to get your gain when you read three and a half pages and then maybe four pages. And if you are pushing that system and that is how you actually stimulate mitochondria biogenesis. So mitochondria biogenesis is the key thing. Now an interesting thing also is physical activity movement has been shown to build mitochondria in all different tissues in the body. It is not just specific for the muscles.

So you mean they find like liver mitochondria concentrations go up when people do physical activity and exercise. So one of the key things is there has to be some kind of movement, there has to be some type of activity tolerable to what the person can handle. You know, and I remember meeting a mentor a long time ago. She goes, listen, do not get sick. You got to get them to move or they will never recover. I do not care if they are thrown in a lake, in a barrel and they are just paddling away or whatever they need to do. I have actually used the analogy that

some patients that had been severely ill just lie on your bed and just move your arms and legs for as long as you can. And then that is it. And then recover and then try to do that several times a day. And as they do that, they are building mitochondria throughout the whole system, like a sedentary lifestyle is going to completely impact the potential for mitochondria biogenesis. But you do not have to be a super athlete, you just have to work to your level of whatever fitness you have and then push it a little bit more. And that causes this hormesis effect.

The same thing with the brain is like if a person damages the cerebellum and they have balance issues and we just have to work on their balance system for whatever level of time they can before they start to get dizzy and then they back off. But if that action doesn't take place like that stimulation to turn on these protein messenger pathways to proteomic pathways to generate the activation of mitochondrial biogenesis, we actually turn on the production of these, people cannot recover. So this is the problem with this supplement game and so forth. Now, there are some people that are so severely mitochondrial compromised where you may have to take down their inflammatory load before they can move and do things right. There are people like I have had patients that say I can not. They go outside to get the mail. I'll be in bed for the rest of the day. I can not do that. And those are like the most severe kinds. For them, you might want to have something that can reduce the load with other factors first and then encourage them to go get the out and get some movement. It is like there has to be some degree of misuse or suffering to these mitochondrial biogenesis pathways. And I think that is one of the biggest things I see neglected in the clinical setting world is an emphasis on everything besides that.

Ari Whitten, MS

This is why I love you, Dr. Kharrazian, and this is why I knew you needed to be a part of this summit. Because this is what you just talked about, is something I have been talking about for years. And it is my criticism, my constant criticism of the functional medicine space, because very few people have understood mitochondrial biogenesis and its importance and the role of hormesis in that. I feel mitochondria have come into vogue now. Everybody's talking about it. But for the most part, the paradigm is that you probably have mitochondrial dysfunction and we will run these organic acid tests and maybe a micro swab test or maybe something else and based on that will determine you have mitochondrial dysfunction. So here's some B vitamins, some alpha lipoic acid, some CoQ10 and some PQQ and that is the solution. That is the protocol for mitochondrial dysfunction. And no, we have so many lines of evidence showing that essentially in the modern lifestyle causes a loss of about 75% of the mitochondrial capacity by the time a person is 70 years old, there is this massive atrophy in the same way that a muscle atrophies if you immobilize it, put it in a cast. It is the same thing that is happening internally at the mitochondrial level. We have to rebuild that cellular engine. And I'm so glad that you have emphasized the importance of hormesis in your answer there. I'm wondering if you can speak a little bit more in depth of the typical functional medicine paradigm of mitochondria and mitochondrial dysfunction and how most practitioners are attempting to treat it.

Datis Kharrazian, PhD

Well, just like you said there, with mitochondria that is in organic acids test or the urinary and I see this beautiful map the lab points out in metabolite it is a mitochondrion and it appears this function like you need to think that that is a ridiculous model. I do not actually remember talking to one of these labs that does. So they go, why are you selling this nonsense? It is so ridiculous. Like, this is not how this works. You are not capturing true mitochondria with your urine output. It is happening at the cellular level. Jumping to like a single nutrient for that is like clinically. Who wrote this? A real clinician never wrote any of this stuff. It sounds like it is very scientific and I think people are drawn with that. There is a point where I just almost have given up on health care practice too. I'm an educator. How could you not critically think, why do you think,

Ari Whitten, MS

So many of them are just protocol followers and they do not think.

Datis Kharrazian, PhD

How do you think the metabolite in the urine tells you what's happening in the cellular space and then what should happen to the patient if they get a supplement overload of stuff. They get all this money spent on extra diagnostic testing. They may not still have any outcomes. Who benefits? Or maybe once someone actually helped them, but is totally unrelated to the lab test. It is just something their body responded to and then it must be working. And I think if a practitioner gets a few of those accidentally, then they will see how it works in a particular manner. I'm not a big fan of the organic acids test. I think most metabolites first of all, from a laboratory perspective, working in labs as a Ph.D. student, are not reproducible. A lot of these markers are terrible. If you measure the person at different times, if you even do the same biomarker the same day, they are not that effective. So if you take someone and give him dice and say, I'm going to give you a dice test, and every time six comes up, I want you to use CoQ10. Every time one shows up, one should use a multivitamin product and someone comes in to go get a six.

And then eventually there are going to be some people that maybe it helps, but it doesn't mean the testing was accurate. So that is just a little frustration. The biggest clinical indication that a patient in mitochondria is improving is their endurance for whatever they could not do improved and their fatigue or if their energy levels themselves can be changed. But the first is going to start with those. So now they can do things longer. They are not fatigued as much, whatever it may be. So that is the key thing and resiliency. So now they can eat maybe a meal and they are not totally passing out. Now they can go three hours down to be on the couch, which is not dropping now. They can lose a night's sleep and they are not getting cold the next day. All these things are resiliency and resilience is a big part of it is mitochondria integrity.

Ari Whitten, MS

I'm so happy to hear you say that because for years I have been telling people that the symptom of fatigue itself, the symptom of lack of resilience, the symptom of loss of endurance, of stamina

are actually more sophisticated, more accurate markers of your mitochondrial function than your organic acids test. And it is hard for people to understand because it seems much more primitive, it seems much less sciencey and sophisticated and cutting edge. But you have to actually be sophisticated with scientific literacy to understand why that is true. So I'm glad to hear you.

Datis Kharrazian, PhD

It must be very

Ari Whitten, MS

Share my views.

Datis Kharrazian, PhD

It must be very frustrating for you to interview all different types of people.

Ari Whitten, MS

It is, often. I'm very happy and, to be honest, a little surprised to hear you say this, not because I have known you for many years now, but because I know you are absolutely one of the most brilliant minds out there. But the truth is that there are many very high-intelligence people who are suckered into bad modes of thinking. If you do not have the right paradigm and you do not have the orientation to think critically and think for yourself, oftentimes you end up following the experts and doing what everybody else is doing and you let groupthink go on. And there is another aspect which I'm sure you might have some comments on, which is within the culture of functional medicine, I think, and also like financial incentives and marketing of all these practitioners trying to market themselves and promote themselves, there is a culture of like one-upmanship where different practitioners are trying to one up each other by having a more sophisticated testing panel and the fancier tests and a fancier sounding methodology and these kinds of things.

And what you are talking about and what I'm talking about here saying, hey, the symptom of fatigue if you have access to it and with a simple questionnaire, just ask yourself that question or your resiliency or your stamina. These symptomatic markers are actually more accurate. That is less sophisticated and from a marketing perspective, sells less well. And so I think that culture promotes this kind of environment where all these practitioners are constantly seeking fancier and more tests of various kinds.

Datis Kharrazian, PhD

That is one of the red flags for me when I see a file come in from another practitioner, if they have done a lot of testing, I'm like, they are new, they do not have to do it. And then like the more seasoned practitioners are doing a very detailed history and then they are making some realistic goals. Read four pages instead of three, do the mailbox command, do not get busy with standards, and repeat. And then those become really noticeable things to monitor ultimately

with just chronic cases. It really is a trial and every game. And I remember talking to congratulate him like, listen, I'm at the point where I do not trust what anyone else says because that an author biases in their ability to interpret the information is having a hard time trusting a lot of research because we as a P-value .05 for every study, which means the study is perfect, 120 are wrong and no study is perfect, then it is like, okay, so even one of this study, we do not have enough like to do a meta analysis. I'm looking at the same piece of information. I look at labs, this lab error, and then there is misguided things that the labs can actually mean. Then you put that all together and then you are like, okay, well, I just have a bunch of stuff that may or may not be effective.

And of course, it is useful to see anemia on a CBC and things like that, but they are looking into more subtle things. Ultimately, you are stuck in a clinical setting with this patient. Can't do these things. What can we do through trial and error, and how can they potentially recover? And if they recover, that is a clue that we are hitting the right pathway. When we do something, that is an improvement. And if they do not recover, then it is also diagnostic meaning that is not where we need to go and then you guys go through the whole process. So I think that is where it really is and ends up anyways. And I think our patients can be very frustrating because they want to get answers right away. There is something very attractive going on. Okay. Oh, I have, I have motor oil toxicity or I have Lyme disease, I have heavy metal toxicity. It is like just these simple things. And then and obviously they can spend thousands of dollars going down that rabbit hole and not really getting any outcomes. And that is what they have to be careful about. Now, I would say when it comes to mitochondria like mitochondrial genesis, the key thing with mitochondria is what we have been talking about getting hormesis is getting activation, getting that proteomic message to actually make these mitochondria and we can all make in, the more movement the more activity we have with cognitive stimulation, we have more challenges. We have to resist what the mitochondria can make.

And then the next thing is really getting rid of unhealthy mitochondria, this whole mitophagy pathway. We have only so much space in a cell, there is only so much mitochondria that can be generated in this cell. And if they are unhealthy and bad, then it is actually going to impair mitochondria, biogenesis pathways, and this and if you look at all the research on Mitophagy, the clearing out of these unhealthy mitochondria is a period of time they just wear out. So as they make energy in ATP, these cells become less efficient and then we have to get rid of them and getting rid of them, not having space for new ones to come in. So if this mitophagy path we were clearing out of unhealthy mitochondria that have kind of worn out over time, is it working? And it is a big problem. And that goes back to just like sleep, like you going to have sleep. I mean, I think people do not realize physiologically the reason we have to have sleep is because we have to use all our energy to get rid of all our debris cells to Mitophagy. So movement activity and getting proper sleep, probably some of the best remedies for any kind of fatigue endurance tissue than any nutraceutical.

Ari Whitten, MS

And have you paid attention to this emerging line of research and especially with Russell Reiter around melatonin and mitochondria? There is been some pretty new and I think I think will when all is said and done 1020 years from now, I think we will realize that this is a really important aspect of physiology. But there is this as it stands now, 2023, it is very new research showing that mitochondria produce their own melatonin. Have you seen this research yet?

Datis Kharrazian, PhD

I have seen it.

Ari Whitten, MS

Interesting. Okay.

Datis Kharrazian, PhD

Have you always been of stuff I have never heard of?

Ari Whitten, MS

Okay. You are going to love this.

Datis Kharrazian, PhD

All right, so it is.

Ari Whitten, MS

It is super interesting. And I think you are going to be fascinated by it. So Russell Reiter is probably the most well-known melatonin researcher. He is an old guy now, but he is been researching melatonin for, I think several decades. And fascinating research shows that mitochondria, it is not just the pineal gland and it is not just the gut that is producing the supply of melatonin. But it turns out melatonin is this critically important mitochondrial antioxidant that also interacts with the internal antioxidant defense system, glutathione, superoxide dismutase and catalase and heme oxygen, and some of those other internal antioxidant defense system to recharge that system at night while we sleep along with mitophagy and all those things that lots of other beneficial things that go on. But it turns out they did experiments in mice where they removed the pineal gland and then they measured levels of melatonin in the mitochondria and they found that in mice with no pineal gland that they still have the same levels of melatonin at the mitochondrial level. And then they discovered that mitochondria melatonin is so important to mitochondria that mitochondria actually produce their own supply of melatonin.

Datis Kharrazian, PhD

Wow.

Ari Whitten, MS

And that interestingly cardiomatic stress, especially exercise, stimulates an increase in that likely to help balance the redox held balance to the oxidants that are also produced and especially red light. So obviously we get that from the sun, but also red light devices stimulate very strongly this mitochondrial production of melatonin anyway. I think it is going to be an important layer of physiology and I'll share the research with you after we get all the wonderful.

Datis Kharrazian, PhD

Yeah, you are welcome. It makes sense. I know for sure as we sleep when the pineal gland itself is producing melatonin, it primes the immune system and activates mitochondrial pathways for fusion vision and autophagy and so forth. But yeah, that is the thing. These are interactive different types of cells. And the key thing is going back to have hormesis, reject stress to activate them, and then you have to have sleep, get rid of them. And if you are not sleeping well and also circadian rhythms just like a general circadian rhythm, are really critical. So the other thing I go through with patients that are having issues with endurance issues, I mean, they want to rebuild their mitochondria is we can get them to move with whatever limitations they have but try to induce hormesis so it is difficult for them. It is not like they can walk. It is no problem. We want to push it a little bit.

So whether it is getting the heart rate up a little bit more, the length of time, something to really push their activity and we want to do that cognitively want to do it physically. There were those challenges and then we really want to focus on making sure they get enough sleep and improving their sleep hygiene, but also trying to get their circadian rhythms working. So we get them in the pattern of just trying to start waking up at the same time, eating at the same time, actually the same time, and just get this as efficient as you can. So for them to recover and I got to tell you, working with people who have brain injuries. And brain injuries are a massive insult to mitochondria and neurons, and that impacts recovery. If we do not do those things, they can not recover. They have to have proper sleep, proper promise activation and normalizing a circadian rhythm to really make that system work. So that is like the starting place for me. And then what we like to do is how do they respond to their activation and stimulation. There is like there is some people who completely crash when they try to increase their armies. It is like working out. Yeah, to me.

Ari Whitten, MS

This was my next question. I'm glad you brought it up.

Datis Kharrazian, PhD

Okay, so then for me, I want to go, what kind? How do they crash and what caused them to crash? So any kind of physical exercise. For me, I start to really think about whether they have any antioxidant reserves. That might be a trial that we might bump up a whole series of antioxidants for them, like green tea, resveratrol, turmeric and or whatever the series of cocktails

off my book acid. And they see and to see if that load over the next few weeks can serve to impact their endurance.

Ari Whitten, MS

Can I interject one thing very briefly? Part of the reason I think this melatonin story is so significant is because it is such a strong mitochondrial antioxidant and because it interacts with that internal antioxidant system. And given that light, specifically red wavelengths of light, which we get from sunbathing, is probably the single most potent source of mitochondrial melatonin. I actually think that what's going to come out of this is that we realize that sunbathing is really, really important. Getting adequate sun on our bodies is much more important than just the vitamin D story that most people think. Most people think, I can just pop a vitamin D pill and then I can spend my whole life indoors and not get sunlight. And the vitamin D has me covered for the benefits of sunlight. And it is like, If you really understand what sunlight is doing to you, you'll understand. There is a lot more layers to that story than just vitamin D. And I think that we are going to figure out that this is a big one. And I think it relates to what you are just talking about there.

Datis Kharrazian, PhD

I think you are right. I think that is going to be huge. I think it is more than just vitamin D. It brings up the point of these antioxidants and these systems, that is another area. So it is not one of the key things that we have to make mitochondria in our system is to clear mitochondria. The other one is that mitochondria are very susceptible to free radicals, inflammatory mediators and so forth. And there are some people that are chronically ill. They just may have their free radical pro-inflammatory load exceed their anti-inflammatory antioxidant load. And in those cases, we will know right away it is not as theoretical as once we put them on a series of those compounds. See, they are going to make a big difference to me not. It doesn't. Then we know that my condition for some people, they may notice some change. It may not be 100%, but maybe 20% or 30% or something. They definitely notice it when they miss it. When they read one of the red flags for me is also when I see my patient come in, they have a list of all the supplements they take and they get, okay, you are stuck on an island. You can only take three cell phones with you. Which ones are you taking? So do not want to take hundreds of 14 and what are the priorities? And if they like, oh, I got to have my next little sustained I have got to have my green tea. I have to have this like these are all in talks like okay, we just need to boost your levels of, and, and then we are pretty much more cautious in the recovery and then that is where you really like for me that is when I go, I really want to take a deep dive into things that a couple of mitochondria their quality in their home that is the huge one for me I always like to check their air quality, make sure that air filters their home base. So then you look at chemicals, but I'm not looking at exotic chemicals. I want to look at the chemical load in their home and then see what we can do to mitigate that. So I always use air filters. I'll try to make sure that they know they are using ceramics and glass and just go for three, or four cookware, bakeware, and storage foods and things like that. So we will go through the whole thing like trying to restore chemicals that way. We may even check chemical levels with different profiles and see if they have any elevated levels in and see if we need to support their biotransformation pathways and go through that.

Now that only happens with a small percentage of people like that is like most of us, not everyone. And I can tell you, if I ran a chemical load profile on a hundred people, I'm going to get 90 back there.

Ari Whitten, MS

Yeah.

Datis Kharrazian, PhD

Since those people have a high chemical load. But there are many symptoms. They have a pretty good antioxidant bio-transformation pathway that even though they have this load, it is not devastating for that. So this is the other variable, the other factor. So then I'll go through and just start to look at what things impact through bioenergetics, like what things really impact their energy levels. So let us assume they are just having intermittent fatigue. So some days are better than others. And they can have a bad day or a good day. So that is what I call an intermittent fatigue patient. If the equations are totally different, then every day is terrible. I can not get out of bed. I can not function. That is a whole different matter.

Ari Whitten, MS

What's different physiologically? Can you?

Datis Kharrazian, PhD

I think a lot of these people have severe autoimmunity. There is a whole list of theories related to mitochondrial autoimmunity, but they have not been able to identify the target protein yet. But it is pretty clear that there are target proteins. There are some mitochondrial proteins that have been published on like people that have severe fatigue mechanisms. But I think some of that is going on and those are really difficult to turn around. It is not just how we try to improve the quality of your life, at least in the clinic setting that and skills I have to try to help them with what I can do as a functional practitioner. Those are people that come in to go, okay, we got this nailed with they get you fixed up. It is almost, you know, and sometimes they do have serious problems. There are some examples of people actually getting mycotoxins exposure. There are people that really do have more toxic than they really get sick from them. They are not as common as people think, but they are definitely there. There is some kind of severe illness like, a micro toxin poisoning or something like that sometimes comes up. Sometimes I had this one person who is working and they would have these buses turn on and he is working in his is managed like an executive in a hotel and every morning they would have a shuttle. He would just stand in front of this gas exhaust in the shuttle and drink coffee with their coworkers. That is a lot of benzene exposure. You just stop that for like two weeks. So I feel a lot better.

Ari Whitten, MS

Yeah, it is amazing down here in Costa Rica, everybody leaves their engine running. When their car is stopped and they are hanging out next to their car, they leave their engine running. Because it is so hot that they want their AC in the car going all the time. But they will sit outside

like when we need to go to the airport or something. We have a taxi come to our house. Invariably, without exception, every one of these people will park in the driveway, get out of their car, waiting for us, leaving the engine running. And so the whole process of putting the luggage in the car and getting it loaded up and all that stuff for 20 minutes, you are like breathing exhaust fumes. So if I do not say anything I will be breathing exhaust fumes. So I have to ask these people every time and they get annoyed with me, of course, to turn the engine off. But imagine somebody doing that job where they are 4 hours every day breathing those exhaust fumes and they do not think anything of it.

Datis Kharrazian, PhD

Well, exactly. So those are the things that you take a deep dive into a car and you start to think about it. And a lot of times, like the patient themselves, they like you really think it is that and like why we try. So try to find any sort of chemical lubricant, especially if they have a lot of difficulty with activation and movement and crash really quickly. And we definitely think of chemical-related issues. Blood sugar is always a big one. There can be a lot of people on blood sugar issues. There will definitely be an impact on mitochondrial functions. You need to have glucose to make ATP. So we will look for the classical symptoms of this glycemia admirable sugar levels by asking how do you feel after you eat? And then all the answers should be not hungry. If they say I feel energized, they can focus, they can think I can concentrate again. And that is a sign they were hypoglycemic, so they may be going along with that eating and have epilepsy mechanisms to address and those they can get really tired of and we think the mass of insulin resistance issues.

And that could be one of the factors where they are not carrying glucose into their cells to feed their mitochondria. A lot of times you get a chronic exacerbation and you get them to move, develop activation of mitochondria, Biogenesis, get them to sleep properly, start to get in normal circadian rhythm, and stabilize their blood sugar levels. And we may not even use any cell phones at all. And finally starting to recover now the list of 100 supplements is like that kind of way. Now, sometimes supplements definitely do help make nutraceuticals do help, but they are never going to work on their own. There is an interesting way to do those mechanisms with mitophagy and mitochondria fusion and make sure you get Genesis and it is just not going to happen. So those are the strategies that we are trying to do. So it is almost really more of a lifestyle medicine approach that there are various factors like people do have a toxic mood and sometimes very about transmission pathways not working, but it is kind of the real game, the real game is not a nutraceutical issue. And there are people that have, for example, do have hormone deficiencies or actually do have hypothyroidism. There are people that have the underlying diseases. No one's diagnosed them with early kidney disease, but they have not run a routine blood test in five years because they do not trust conventional practitioners and they are only seeing alternative and alternative people typically do not do any routine lab work. I mean, I see a lot of that in my practice. I see the referral from one person to the next, the next. And no one's really had a real good workup. They just kind of walked into their five-minute medical

appointment and they even showed abnormal signs of kidney disease or yeah, some kind of actual hepatitis.

No, come back. We will check it again later. And like, they never go back or it gets ignored. And then you are like, what a Pango you have hepatitis C, you have like stage two kidney disease. No one told you for such a long time. So I think that happens with more people that do not have fatigue. They are just tired all the time. Yes, I think ruling out actual pathology is a key factor that gets overlooked. Well, there are some people that have malignancy, early stages and the immune system failing white blood cell counts, drop natural killer cells B really high or low. So we will do a liquid biopsy like a gallery screening test to see if they have any fragments that'll screen for like 80 tumors at once. And even at times, we will do a full body MRI scan. And studies have shown that it is been very effective to finally tumors without the radiation exposure. So it is a red flag. So for me, it is intermittent fatigue, some basics better than others. And then we will look more like the physiological lifestyle mechanism. If it is fatigue all the time, then we get to rule out disease, rule out pathology. And if they are really pathologically fatigued where they just can not function at all, then we are really thinking that they may have these more progressed mitochondria autoimmune type responses. And then the goal is really to try to improve quality of life with whatever we can. In that case, we might come up with different nutraceuticals to see whatever we can get and just trial and error and kind of rookie through it. So that is how I approach it.

Ari Whitten, MS

I want to add one layer of ease of context or addition to this story that you have mentioned or this way of looking at things. There was a paper that came out maybe ten years ago or something like that, and it was basically evidence-based guidelines for physicians to treat their patients with chronic fatigue, I'm going to say evidence-based, quote unquote. It was published in the Journal of the American Family Physician, and it said, how physicians should treat their patients with chronic fatigue or look to diagnose them initially, runs a standard blood test. And they specifically said in 95% of cases, there is nothing found on those tests. In patients with chronic fatigue, nothing found that explains their chronic fatigue. So 95% of the time you are in the categories that you have just outlined, maybe five percent going to be in that category where there is some serious underlying disease. 95 out of 100 people who are complaining of fatigue are probably going to think you are not going to any serious underlying pathology or disease that is present.

Datis Kharrazian, PhD

Yeah, absolutely. I would say that as in your population sample too, but if you had a population sample of a person being chronically sick for a long time and not having a routine workup for a while, maybe it is seven and a half percent. Maybe it is not five percent.

Ari Whitten, MS

No. Well, in your demographic, like you have established yourself in this unique niche where you are like the most brilliant functional medicine practitioner, who trains the functional medicine

practitioners. So you are like the last resort after somebody who's been to five or ten or 20 other practitioners and nobody can help them and nobody figures it out. It is now I need to go see Datis, he is the guy. So I'm sure your percentage is probably like 50% some underlying serious disease.

Datis Kharrazian, PhD

But it is but most of these people, like you said, just have like these little things that they are not going to show up on routine lab work. They do not have disease. Are there physiological things that we do not have parameters to look at? And obviously, the organic acids and some of these functional medicine tests are going to capture that. Ultimately it goes back to. Do you have more endurance? Is your endurance level changing what interventions to be done that are changing your endurance and your energy levels? And that is like the biggest thing I always do when I work with my patient population, I would say, listen, it is chronic. This is an emotional endurance game where we have to make a plan, write it down, check things off, circle things, go through a stuff list. Let your body tell us with the right response is. And unless we can go through that or there is no way we can figure it out. And sometimes you get lucky and sometimes it takes forever and sometimes, as a practitioner, times I work with a patient and go, I'm totally failing you. I do not know what else to do. I'm really sorry. Like what? You just saved my life.

And I'm like, What? Every day you are still complaining all the time. They are like, No, no, my quality of life is gigantically better. And then, okay, well, then that is good. So it is difficult. And I think for people that are suffering from mitochondria issues, chronic fatigue issues, a lot of the treatment is in your hands. You really can activate, you really can try to focus on your sleep. You really can not try to find things that are like, for example, a person can not sleep. The question is why have you sleep CT? Do you have sleep apnea? Yeah. Frequent urination. For some reason, you have an overactive bladder at night. Do you have a prostate issue? Do you have poor bladder muscle tone as you have gotten older? They do contract and do some people exercises or I mean, like if you can stop urinating at night, five times a night, you can actually start getting rid of this mitochondrial debris and you can start to actually recover from your health. And trying other pathways, too, so that they can sleep. But those are like the fundamental things. And as a person, as you said, who sees others some of the cases of the practitioners have referred to me, it is rarely ever. You did not take this supplement. It is always like our only goal in the next two months is to see if you can sleep from three hours to six hours, nothing else. That is what we are focused on. So if we can not do that, we can.

Ari Whitten, MS

Yeah. With that in mind, I want to just loop back to that paper I was just referencing, and the reason why I said quote unquote around evidence-based is as, as far as again, these are guidelines for physicians to treat chronic fatigue.

Datis Kharrazian, PhD

Yeah.

Ari Whitten, MS

Patients with chronic fatigue. They offered four treatments.

Datis Kharrazian, PhD

Okay.

Ari Whitten, MS

Number one was a recommendation to walk for half an hour a day. Okay. I have the least problem with that one. Yeah, they had cognitive behavioral therapy, they had antidepressants and they had stimulants as needed antidepressant drugs, and stimulant drugs. Those were the only four treatments discussed in the paper for these so-called evidence-based guidelines to give you to emphasize this, nutrition is not mentioned at all for medical stress and mitochondrial biogenesis is not mentioned at all. Mitochondria are not mentioned at all. Sleep is not mentioned at all. Circadian rhythm is not mentioned at all in this paper. Toxins not mentioned at all. None of these things are mentioned at all. So this is really a paradigm issue. This is a conventional medical paradigm seeking drug cures for diseases. And this stuff that you are talking about is not even within them, they do not even really have the right conceptual framework to even think about these kinds of things in the right way.

Datis Kharrazian, PhD

No, I know it is very frustrating. There was a survey, the answer function that I do not know 15 years ago was a long time ago. And they asked the medical physicians that jumped into functional medicine, why are you here? What was your motivating factor for functional medicine? And the number one answer was They got sick or a family member got sick, and then they are like, I do not I'm not thinking through this the right way. I do not have the tools. It is not disease-based, physiology, functional based. And I think things are changing. I think, you know, the people are demanding more information are getting out there more. But the other thing about functional medicine is that it is a patient treatment or a patient model where we need an active participant. It is not like a passive model. Here's your beta blocker. Use your ACE inhibitor, just do what you are doing. Lacie Blood pressure control. Here's the next polypharmacy list of things that you need to take. It is really like, okay, you have got to sleep, you have got to move your skin rhythm. You have going to reduce your toxic load and they are kind of going through the whole process. So for me, it seems like the patient population that is attracted to functional medicine is highly intelligent. They are critical thinkers, and they are looking deeper because they realize, Yeah, I do not have disease, but I do not trust them anymore. And unfortunately, it is led to mistrust and now they do not get conventional workups. And then we get, people disease that it is an ugly mess. But the people mentioning it are exactly right.

Ari Whitten, MS

You know what's interesting and I love this conversation. I always love talking to you and I always come out of it smarter and learning new things. But what's really cool and.

Datis Kharrazian, PhD

I learn a lot over time.

Ari Whitten, MS

That is cool. Thank you. That is a great honor for me to hear that from someone like you. But what's really cool to me is I perceive this whole landscape of the medical paradigm and studying disease, studying pathology, and there it is like real, endless, infinite complexity that you can go down with studying this disease and that disease and what are the specific biochemical mechanisms. And there is constantly new discoveries of some new layer of abnormal biochemistry associated with this disease and that disease and the whole focus of medical paradigm and even lots of people within the more natural and functional medicine is to delve more deeply into understanding the intricacies of all this abnormal biochemistry with the idea that eventually when we understand that deep enough, we will find some intervention in whether it is a drug or a nutraceutical that interrupts that pathological process, that abnormal mechanism, and that will create health.. And what I love about this conversation here with you is hearing you talk about essentially lifestyle medicine as the central thing that someone needs to get better. It is like you are more than anyone. You are more brilliant and more knowledgeable about all that crazy, detailed biochemistry of all these different disease processes, but 500-fold more than I am. And yet you are coming back to essentially a lot of the same recommendations that I'm arriving at without having spent so many years delving into all of that. The study of all the complex biochemistry of disease processes.

Datis Kharrazian, PhD

Well, I think there is an ultimate truth. And I think when you are actually looking at working with people that are ill, the truth is going to be what works. It is not going to be like these theoretical models of this molecule for this. And at the end of the day, I think the difference in models also when you look at the and then of course, I'm not into medicine, you are an anti-medicine. We're going to miss it. We're just critical thinkers of how that was being approached. But when you look at the top prescriptions, you know, beta blocker or ACE inhibitor, HIV Curtiss inhibitor, proton pump inhibitors, everything is blocking and inhibiting. We do not give up and things turn on things and things that turn on things are like we talked to hormesis and sleep and lifestyle, things that make a difference. Now there is definitely a place for nutraceuticals too. It is just it never supersedes the other variables that are more lifestyle based. But this then there are some people like I have had some patients who were like they can not sleep, they may be poor reason, they can not because they are hypoglycemic all day and they just do not make enough glycogen to they can not get through the night and we have to empty it maybe to protein at night and then sometimes like they can not shut down a little bit, we may have them give me a little bit of valerian to help them start to initiate that circadian rhythm.

And they will start to sleep and then we will start to have monitors that can rhythm, they can start to get out of the rut that we used to. We did not use it. We used a GABA agonist, something

very natural, and non-addictive to try to get some sleep, some functions. So, a combination of those things is part. It is not like one is that we need to do the little thing but fundamentally it is trying to improve physiology, improve function. If someone was really ill and they moved as much as they were able to, they got sun. They were unhealthy people that they love to be around socially. They laughed. They get to have a sense of self-worth. They get some acceptance. They eat real food. They sleep well. They are probably going to be healthy. Yeah. So it is those things that get the story where things go wrong.

Ari Whitten, MS

Yeah. Absolutely. Dr. Kharrazian, I absolutely love this conversation, one of my favorites of this entire summit. And it is always a great pleasure and honor to speak with you. Are there any final thoughts that you want to leave people with? Maybe especially for people dealing with complex, chronic illnesses who have been struggling for a long time? Anything you want to say to them?

Datis Kharrazian, PhD

Well, I would say you can do a lot of things on your own like you do not have to. First of all, do not be passive, you won't get better. If you are a passive patient and just want to have someone recommend things for you, you won't get out of chronic disease. Getting out of chronic disease requires active participation on your part. So if you are fatigued and tired, the things we talked about are really critical. If you have chronic pain, you have chronic fatigue issues, you have to get some movement in. You do not have to go and run a mile or something. You just need to do whatever movement your body can handle. And then just a little bit more in the arms of that will have a profound impact, especially if you monitor it over one week, six weeks, eight weeks, and 10 weeks to see what it does to your system. Physiology. It will be painful and difficult emotionally every time you have to do it, but that is really kind of what it takes to pull through with it. And if you could just get that in and then really try to figure it out if you are sleeping while we can do for sleep and maybe the reason you are on the summit is because you have mitochondrial issues and fatigue and exhaustion issues and you can not recover. And those two little things that you could control that no one else can be profound.

Ari Whitten, MS

There is one thing I want to draw attention to that I love about the way you have talked about things is self-experimentation. You have talked about as a practitioner that you are kind of going through this deductive process of figuring out maybe it is this, maybe it is that, let us experiment with this, let us experiment with that. And I want people to hear that Dr. Kharrazian is one of the most brilliant minds in all of medicine. And he doesn't have, like, I have got the answer. You just do step one, step two, step three. And I fix everyone instantly. It is a process of figuring things out. And as individuals listening to this, what I want to get across to you is you should also be seeking as much knowledge as possible, become as scientifically literate as possible, and operate from the principles and the paradigm that is been outlined here by Dr. Kharrazian. And then try to have an attitude, a positive attitude, being as he said, proactive about trying new things and

experimenting and being part of your own solution rather than just sort of being a passive patient.

Datis Kharrazian, PhD

So I would say one last thing. Yeah. The one key factor I have seen in my career I have seen really makes a difference for outcomes unrelated to the disease is the sense of purpose. And now there is all this new research on longevity. That is a key factor in longevity, too. You get also to make an issue of a sense of purpose.

Ari Whitten, MS

Yeah, yeah, absolutely. Dr. Kharrazian, where can people find you? Follow your work and keep in touch with you. Where do you want to direct people?

Datis Kharrazian, PhD

I just have a website called DrKharrazian.com. That is the main place to go if you are interested in the things we are doing.

Ari Whitten, MS

Thank you so much, my friend. It is always a pleasure to chat with you and I look forward to the next one also.

Datis Kharrazian, PhD

Awesome. Thank you.