



EVERYDAY IMMUNE RESILIENCE

Datis Kharrazian, PhD, DHSc, DC, MS, MMSc, FACN

Hi everyone. Today's topic is going to be on fatigue, so what I'd like to do is maybe spend the first 10-15 minutes trying to give you some of the basic concepts that are associated with fatigue and discuss what some of the mechanisms that cause it, and then what are some clinical strategies you can use if you're dealing with fatigue.

For the most part, the key thing is that when you're looking at fatigue, when you break things down ... As a clinician, when you have a patient that comes in that says they have fatigue, the first question you're trying to figure out is, what's happening? What's going on? When you first start with fatigue, you look at the cellular mechanism and in the cellular mechanism what you're trying to do understand that energy production is a set of functions involving cells called mitochondria. These powerhouse energy producing cells called mitochondria make sometimes called ATP and ATP is basically the fuel for all our cells and all our biochemical processes.

At the end of the day, when someone says they have chronic fatigue and that they're tired, then what we know is that this mitochondria is not doing its job. Now, it may not be doing its job because there's not enough mitochondria there. It may not be doing its job because there are things that are disrupting mitochondria function, the biggest one being inflammation or it may not be doing its job because it's not getting what it needs and it needs oxygen and it needs fuel, glucose, to really make it work. From a clinical scenario and from a pathophysiological scenario, when we see a patient that has fatigue, we're trying to go okay, now all we know is this mitochondria is not working efficiently.

The next questions you want to clinically ask is does this fatigue happen at certain times of the time or are there things that trigger the fatigue? Is the fatigue happening all the time. Those then help figure out what's causing the fatigue. Then there's people that get labeled as chronic fatigue syndrome that may have chronic patterns of fatigue and a lot of times they don't really figure out why. Let me go over some major concepts.

The first major concept is that you have these mitochondria. Now, mitochondria are produced in their cells but the key thing to understand about mitochondria is they also go down, our production of mitochondria, so we have a mechanism called mitochondrial biogenesis, which is there to help us develop these powerhouse factories in our cells so we can make energy. But every decade of life our mitochondria go down by some degree, by some percentage point. For some people it could be 2%, for some people it could be higher, but every decade we start to have less mitochondrial biogenesis, so we have less potential for energy. This is why as we get older and older, it's harder to recover from workouts, it's harder to have the endurance to do some of the things as when we were younger, and that has in part to do with our normal aging process where we tend to lose some mitochondria.

Now, we can also build mitochondria, so there's a mechanism that's called mitochondrial biogenesis, and remember, the more mitochondria you have, the more energy you have. Mitochondrial biogenesis occurs by actually activating your cells and the biggest players of mitochondria development are your muscular system, your muscles and your brain. If you're constantly exercising and physically active, you actually turn on your gene expression to actually build more mitochondria. This is also why if you're sedentary, it's really hard to maybe start to work out, but once you start working out, you have more and more energy and if you start to follow that routine, pretty soon you have a lot of energy. What's

actually happening is you're actually making more mitochondria in your muscle cells, so that's called mitochondrial biogenesis, which is fascinating and amazing that process can take place.

The same thing goes with your brain. If you stop using your brain, you have less mitochondrial biogenesis. When I say your brain, there's different aspects of your brain. For example, your frontal lobe is executive function planning, organization timing. Your cerebellum is involved with balance, stability, motion, movement. Your auditory cortex is involved with sound discrimination, appreciating music. Your right hippocampus is involved with finding directions, shapes, and images. Your left is involved with numbers and recall. You can have degeneration in certain parts of brain because you stop using them. If you stop doing math, you're going to do build less mitochondria in those areas of the brain and that's the area that's also going to degenerate from lack of use.

Your brain and muscles have the concept as if you use them, you have greater function, but if you stop using them, they start to degrade. One of the key factors with that is the amount of mitochondria that's there. If you're constantly using your brain and active and focused and concentrated, you're going to definitely activate your frontal lobes. But if you're not playing sports and you're not doing things to really stress your balance and your stability systems, then other parts of your brain can degenerate. The key thing is you want it to be very active. When you look of people that have lots of energy, there's one thing they all have in common, they're very active and the fact that they're very active is helping them make mitochondria. When you look at people that are totally run down and tired, they start to get in this pattern of being sedentary. Then what happens is, they're not developing mitochondria, their mitochondrial biogenesis goes down, so they tend to fall apart.

As a clinician, when I see a patient come in with chronic fatigue, my first thing is how do I get them to move? How do I get them to get some activity because there's really no nutrients that have been shown to turn on mitochondrial biogenesis or produce mitochondrial biogenesis. Let me explain what I mean by that. There's some nutrients that have been shown like antioxidants that can turn on the cell messengers to help develop more mitochondria. The bottom line is, the less inflamed you are and the higher antioxidants you have in your diet like healthy polyphenols from different plants and fruits and vegetables and different super foods like acai and pomegranate and so forth. Those things help to turn on messenger protein pathways that help to develop mitochondria. No studies have actually shown that they actually make mitochondria. It's just means the potential to make more mitochondria is there.

Then on the other side of things, the other key thing is you actually have to move and activate. They've done studies where people move their arm and they measure, they do a biopsy of their muscle cells. They get a percentage of their mitochondria in their muscle cells. They have them do physical exercise and activity and they do muscle biopsy again and they see levels going up. They've done similar things in animal studies with the brain where they activate regions of the brain with different tasks with animals and they can see the mitochondria density improve.

We know that activation in use is one of the key things. When you see a patient that has chronic fatigue and they just completely become sedentary and stop doing anything, they have zero chance to get out of it. As a clinician, you're trying to figure out how to figure out what's causing their fatigue, but then as soon as possible, you want them to use their body, you want them to use their brain, you want them to get active as much as they can. They kind of have to push it. For some people, it's starting with a five-minute walk and that's all they can do, but there has to be some type of motion and movement because these mitochondrial biogenesis pathways don't develop unless you can turn them on with activation, not with a supplement and not necessarily with diet. Supplements and diets are helpful with the setting

of the stage, but you actually have to use your body to develop more mitochondria. The more mitochondria you have, the more energy you have. That's one of the other key concepts.

Now, in the real world ... By the way, thank you for everyone who is joining in and saying hi. Wow, we have people from all over the world, which is fantastic. Thank you for those. I'll get into all the questions in one sec, just let me give you some background information that I think will really help you understand chronic fatigue and chronic fatigue syndrome and these types of related mechanisms.

Now, when you look at the big picture, there are people that have really simplified chronic fatigue. They say all chronic fatigue is Lyme disease, all chronic fatigue is mold, all chronic fatigue is whatever. That's a very inefficient way to practice. When you really look at the mechanisms that cause chronic fatigue, you're looking at, you have these mitochondria. How much do you have? The more activation and movement you have with your body and the more cognitive activity you have, the greater potential you have for developing mitochondria. Then your mitochondria has to produce glucose, it has to get glucose and oxygen, so proper circulation, proper blood flow. It needs hormones, proper hormones, especially things like thyroid hormones, reproductive hormones are all in play. Then the mitochondria, in the steps that involved to make what's called ATP, the fuel source for your cells, this process called oxidative phosphorylation and it can be uncoupled or dysregulated or dysfunctioning with basically inflammatory mechanisms, different pollutants, different inflammatory mechanism.

At the end of the day, when you're trying to figure out why someone has fatigue, then you're looking at the rate of how much mitochondria are they producing, the rate of mitochondrial biogenesis, how much oxygen and fuel are they getting to the mitochondria, how much antioxidant reserves they have, and how many things are uncoupling in the mitochondria. If this shifts to the point where someone is chronically tired all the time, then you know that you have to make sure they can get plenty of oxygen and have healthy amounts of circulation to get fuel to their cells. They need to have proper amounts of glucose and glucose stability to optimize their energy function. They need to reduce their inflammatory mechanisms and you have to find any kind of pollutant or environmental compound that can be involved with also uncoupling in the mitochondria to shift back their energy levels. These processes are very effective.

Some people assume that if you just give nutrition for the mitochondria, the most popular ones are CoQ10 and B vitamins and things like D-ribose that everything is going to work better. In most cases, it doesn't do that. In most cases, unless you can figure out the underlying mechanisms, that's really important. Now that you have this background information on the physiology of energy production, let's talk about how this applies to a clinical setting and then I can take some questions.

In a clinical setting, that's the background thought process as a clinician that I think about. If a patient is suffering from chronic fatigue, those are things that you have to also consider for yourself. Then the questions that come up, is like when does a person have fatigue? This is really important. There's different types of fatigue. For some people, fatigue only happens after they eat. That's really when they notice their fatigue. For some people, they have fatigue when they first wake up in the morning and as the day goes on, it gets better. For other people, they have fatigue if they get too much stimulation, like if they're in a crowded environment or if they watch a movie that has lots of action, that causes a lot of fatigue. For other people, they may have fatigue only being in a damp building. We talk about this with people who have mold sensitivity, so there's a trigger.

One of the first things to really figure out is what is causing this fatigue. Let's start with the most common one. The most common cause of fatigue ... By the way, people that have chronic fatigue

syndrome they don't have one thing, they have multiple factors that are causing their fatigue and what you have to clinically do is slowly take things off one by one and shift them to a state where they have more mitochondrial biogenesis, reduce inflammation, reduce fuel that reach the mitochondria, and to kind of break this apart. This model I'm teaching you is a model that's not based on symptom treatment, it's based on understanding the pathophysiology and then working your way through it.

One of the first questions to ask is, do you have any change of energy if you eat? This is one of the first questions I ask my patients that have chronic fatigue. The answer that is normal is that there is no change in energy after you eat food. Now, what you typically hear is with people that are hypoglycemic meaning that their blood sugar levels drop throughout the day, they'll tell you, "When I eat, I feel better. I can function again. I can think clearly. I can focus. I can concentrate." Those are things that are telling us that they have a low blood sugar pattern. If you have low blood glucose, you're not going to have energy. If you have low blood glucose, your cells in your brain are not going to get what they need to make this ATP to allow you to function properly. There are a lot of hypoglycemics out there.

By hypoglycemia, I mean a functional hypoglycemia. It's not that their lab tests are so low that they have a disease state, it's just that the way they're eating, their blood sugar levels are dropping to the low end of the normal range throughout the day and because of that they get shaky, lightheaded, irritable, and for a lot of people that are hypoglycemic, that's when they determine it's time to eat. They go, "I'm really cranky, I can't focus, I can't concentrate." When that's their signal to eat, that is probably one of the key factors in the cause of their fatigue. You really want to first figure out if you're getting energy after you're eating, and if you are, then you need to eat more frequently.

The biggest problem hypoglycemics have is they don't eat unhealthy food, so they think their diet is great. With most hypoglycemics in my clinical practice, I go, "How do you eat?" They go, "I eat great." They eat healthy food choices. The problem is they're having a fruit smoothie for breakfast or a yogurt or tea and honey or a fruit salad for lunch. They tend to be eating lots of fruit and not getting enough substantial protein or fat in their diet or fiber to really stabilize their blood sugar levels. These are smoothie fruit kind of meal types of people or they just miss meals.

If you have chronic fatigue and you're tired all time, if you're hypoglycemic, you also have zero chance of improving your energy levels until you eat more frequently and stop eating high sugar foods, even natural sugars, as your meal. A lot of people think I eat zero calorie chocolate or muffin and it has stevia in it. Just think of stevia and natural things as sugar. It's going to disrupt your blood sugar stability balance.

The other key thing with fatigue is when you're looking at from how a person feels after they eat, another major cause of fatigue is people get tired after they eat instead of getting energized. That's a sign that they have insulin resistance. Insulin resistance happens when you eat a meal, your pancreas will secrete something called insulin to allow the glucose from your fats, proteins, and carbs that you've ingested to get into your cells, so then you can then have that glucose activate your mitochondria to make ATP. People that have a diet very high in carbohydrates or very high in sugar or so sedentary that they don't use their muscles, they have the tendency to develop insulin sensitivity, insulin resistance and in those scenarios when they eat, they just crash because they can't get that glucose into their cells and that glucose that's in the blood actually has to be used and get metabolized so it gets converted to fat. The conversion of glucose to body fat is going to demand energy, so they get really, really tired after they eat.

One of the major causes, one of the variables of a lot of people that have chronic fatigue is this blood sugar instability. Some people have both. Some people get shaky, lightheaded, irritable, they eat and then they pass out. They have a blood sugar rollercoaster ride. In those cases, you really have to cut down on your sugar and carbohydrates and really get your blood sugar levels stable. That's one of the key factors of fatigue.

Some people don't have fatigue after meals, they just have fatigue when they use their brain. This is one of the earliest signs of neurodegeneration. This is one of the earliest signs you see with people who have really poor brain function. They'll tell you things like, "I'm okay on weekends." In a clinical setting, they'll say, "I'm okay on weekends but during the week, I just get so tired." Then you start to dig into like, "What are you doing during the week?" You find out when they get to work, just the drive to work is causing them to get tired. Driving is a brain activation stimulus. When you have to read, when you have to focus, when you have to concentrate, when you have to look on a computer screen, when you have to do tasks that require executive function or cognitive function or recall, those are all things that are brain related. For some people that have early brain degeneration, their fatigue comes on whenever they use their brain, and when they get a chance to not use their brain as much and rest and not have so much stimulation, they're not as tired.

For some people that have early neurodegeneration, just going into an environment where their brain is really called into action like a crowded grocery store, a crowded mall, or a crowded environment, and there's motion and movement and sounds and all those things happening, that can really make them really fatigued and run down. That's a whole different approach. Now you're looking at a person with brain degeneration and there's a whole list of factors that you have to deal with to impact their fatigue.

There are some people who wake up and they have fatigue only in the morning but as the day goes on, they start to function and feel better. Those are people many times you see that are not sleeping well. They're not getting the deep REM sleep. They're not getting enough oxygen to their brain when they're sleeping. Sleep studies can be very helpful for them. They may need a CPAP machine but there's factors involved with their ability to get proper sleep. Then there's people that may have fatigue when they get exposed to chemicals or to a mold building. Those are things that people that inflammation that's driving their mitochondria pathway. Then there's people who have fatigue all the time. For example, they have fatigue no matter what happens all the time every time. That could be several things. That could be a significant underlying metabolic disease like they have hypothyroidism that was never diagnosed, they have chronic inflammation like an undiagnosed auto immune disease patient and that chronic inflammation continues to disrupt their mitochondria so they can't produce ATP, or they have significant deficiencies in their hormones, it's a combination of things.

Now, in a really clinical setting, when you're dealing with patients who have chronic fatigue syndrome, there is no single nutrient that is going to make a difference. You really have to look at these pathways that are involved and then you try to calm down their inflammation. Maybe you have to improve their blood pressure, so they get more blood flow to their cells, they have greater energy, you have to maybe stabilize their blood sugar levels, you have to look at environmental triggers, and as soon as they start to respond to that, you immediately have to get them to move because movements is one of the only things that really develops mitochondrial biogenesis. Whether it's a five-minute walk to a 10 minute walk and so forth. Those are all the key factors that are involved with really making a difference for figuring out how to manage and treat fatigue, so it's a big thing.

The most common things I've seen in my practice with patients that walk in from either the patient not really clicking with the concept or the patient may have seen lots of practitioners and they haven't really

figured it out is really the blood sugar component. It's a big deal. It's typically overlooked. Another major cause is lack of movement. The most interesting thing is people that have fatigue it's like, "I'm too tired to go for a walk." You're like, "Yeah, that's part of the mechanism but you have to at least do something to get mitochondria developed. If you do no activation and no activity, you cannot get out of this. You cannot break out of it."

It would be just like someone who broke their arm, their arm was in a cast for three months and the arm is atrophied. They say, I can't move my arm. Well yeah, you don't have enough muscles. They're like, but moving my arm is too tired, so I'm not going to move it. If you don't move your arm, you're not going to have that muscle grow. It's the same thing with the metabolism of fatigue. You have to have motion and movement to make a difference, to make this work. Okay, those are the main concepts with fatigue.

The last thing I want to talk about things like whether you call it chronic fatigue syndrome or whatever the thing is, I don't know what to tell you, those are just general terms. The other thing to understand is when you have chronic fatigue, especially if your mitochondria in your muscles are not working, you are going to get muscle pains. One of the chronic features of chronic fatigue syndrome is you have muscle pain, you have trigger points all over your body. That will happen when there's not enough mitochondria in muscles. Your muscles have to have mitochondria to produce energy and if they don't have that, they're going to develop lactate and there's going to be constant stiffness and pain in muscles, so it's just part of the mechanism. Okay, let me see if I can take some questions here.

From Susan, you mentioned losing mitochondria if you're older. Are there ways for those of us, say over 40, who want to increase our mitochondria that are different or in addition to what you are recommending for younger folks?

Right, so if you're older ... The question from Susan that we talked about mitochondria and how to develop mitochondrial biogenesis and is there a difference between exercises or things to do for older versus younger people? No, for the most part, it's really the same. If you're older, you might not be able to go for a run, you may be only able to do a walk. For some people, they can't even go for a walk. They may just have to stand up and just do some squats several times throughout the day or do some pushups on the knees. But there has to be some motion and movement and there has to be an effort to try to improve that over and over again and increase their level of demand over time. That is essential to develop mitochondria.

Could fatigue stem from one, from your body fighting EBV?

Yes, could your body develop fatigue from Epstein-Barr virus? Absolutely. Viral infections, chronic infections, what they do is they activate your immune system or basically, your inflammatory response. When you're constant fighting an infection, you're releasing things like interferon to improve activation of natural killer cells to fight the infection but things like interferon and also other cellular messengers called cytokines, they get activated in the immune response and these actually uncouple the mitochondria, which means make the mitochondria not be able to process glucose very well, so that leads to significant fatigue. In some cases of chronic fatigue, you're actually dealing with the mechanism of inflammation or immune activation and it could be a viral pathogen.

One of the biggest clues to you that you may have a pathogen is just look at your routine blood work and see if your white blood cells are normal or abnormal. A common thing you see out there is people that have white blood cells that are low and they go, "Oh, I've always had low white blood cells and that's kind of been ignored." There are people that have chronic viral infections, especially with things like Epstein-Barr that constantly go into remission and relapse, and remission and relapse or they have

an undiagnosed hepatitis C virus and they're always tired and no one has really dug into a viral mechanism. Viral mechanisms can absolutely uncouple the mitochondria and cause fatigue.

Okay, so in that, Joanne asks, **would your approach to fatigue be different for Epstein-Barr than Lyme than mold than toxic exposure, etc? Or is there a basic approach that can be helpful no matter pathogen or toxin triggered the fatigue syndrome?**

The question is, whether someone has mold or Epstein-Barr or a different pathogen or Lyme, is there a different approach to manage fatigue or just do a general approach? This is why most people with chronic fatigue syndrome don't get better because they don't work with a practitioner that understands the diversity of all the things that trigger it. This is why a lot of functional medicine practitioners are very successful working with patients that have fatigue because they're looking at all the different factors. They're not looking at it as a disease that needs a single treatment. They're looking at the treatments that underlying them may be involved. You would handle an Epstein-Barr patient differently than someone who has for example, mold activation for their chronic inflammation and immune trigger presumably mechanisms.

But at the end of the day, there could be some general concepts that you do for all people that have an infection or an immune trigger, which is put them on high amounts of antioxidants to give them some relief but you still have to really address those issues. Also realize that when you start to move and get motion and activity, as you build mitochondria, you have more ATP to fuel your immune system. Your immune cells that are fighting infections also need ATP. When you're completely sedentary and just not moving and not doing anything, they you're not making enough mitochondria, you're not developing mitochondrial biogenesis, so this is one of the biggest factors where people turn around the corner with chronic fatigue or not is getting to the ability to push themselves to get some motion and movement and activity, as little as they can but some of it to really start to break this vicious cycle.

Is there a specific test for chronic fatigue syndrome, lab test?

Is there a specific test for chronic fatigue syndrome? No, unfortunately there's no lab for chronic fatigue syndrome. This is why there was such opposition for the diagnosis of chronic fatigue syndrome in healthcare because they were like, how do you even prove it because anyone can walk into a healthcare office and say I have chronic fatigue. The list of criteria they made over the years where if you have a cluster of symptoms, they you can be diagnosed with chronic fatigue syndrome, but for the most part, that's just basically mitochondria failing and then at the end of the day, you have to figure out what's causing the mitochondria to not develop or why it's uncoupling or why it doesn't have the substrates it needs to function properly.

Okay Carla, **could you please recommend how you would supplement iron for a high school female distance runner with a ferritin of 19? Would you go with IV infusion or oral supplements? If oral, could you give advice on the type?**

I think the question was on iron supplements.

Yeah, ferritin is 19.

Ferritin is 19? Okay, what else?

That's all she said.

If your ferritin is 19, that's not a sign you have iron deficiency. You really have to have TIBC. There is a large group of functional medicine, nutritional practitioners that quite honestly do not understand how to read ferritin. Ferritin is an acute phase reactant. Ferritin levels will go up with inflammation. If you actually have iron deficiency ... There's different mechanisms of iron depletion. Let me explain this. If you have iron storage depletion, like you don't have enough iron storage in your body, than your lab ferritin levels will be below the lab range. When I say below the lab range, I mean in the level of three, four. That just means you don't have iron storage. It doesn't mean you're iron deficient. It still means you have iron in your body. You're still able to produce healthy red blood cells. The times where you clinically have issues with iron deficiency, the lab marker isn't ferritin, it's TIBC. If you really think iron may be a cause of your iron deficiency, the best early marker is actually not serum iron or iron saturation it's total iron binding capacity.

If total iron binding capacity goes up, then it's clear that you may have some iron deficiency. Iron deficiency alone isn't going to cause fatigue. In order for iron deficiency to cause fatigue, you have to have enough significant deficiency where there isn't enough iron to support red blood cells. At that point, you'll see the hemoglobin, hematocrit, and RBC drop. Really, when you're looking for a mechanism for iron deficiency cause for fatigue, it actually isn't low ferritin, it's actually when you start to get early patterns of anemia and that's when you really have a clinical mechanism of fatigue that is relevant.

Kathleen, how do you start to evaluate for neurodegeneration, I.e. fatigue with mental activity.

Kathleen says how do you start to evaluate for early neurodegeneration?

Because you have fatigue with mental activity.

First of all, if you have fatigue with mental activity, you could just be in a low blood sugar state. You could have just not had sleep. Remember, your brain has mitochondria, so if they don't have enough chance to recover and rest and have fuel, it doesn't necessarily mean you have neurodegeneration. However, if you notice your fatigue is always, always initiated and that's the main cause of your fatigue is that when you try to use your brain you get tired or when there's lots of stimuli, things that are activating your brain whether it's sound, light, motion, movement, whatever it may be, if that's causing you fatigue, that's a really big clue that you have some potential early neurodegeneration.

if you guys get a chance, check out drknews.com it's my website D-R-K-N-E-W-S, I have lots of articles on brain health and brain degeneration and auto immunity and inflammation. I also have a free immune resilience program you can download, which talks about lifestyle factors you can use to support your immunity during this pandemic. I also have some online programs that are available if you're interested in learning how to support your immune tolerance system, which is important to modulate your inflammation and your immunity. I also have a program called Save Your Brain, which is a six-week program where I teach all the lifestyle and dietary concepts to really improve your brain function. If you any interest in those, please check those out.

I also wrote a book on the brain, *Why Isn't My Brain Working?* In that book, each chapter I talk about different mechanisms involved with causes of brain degeneration like blood flow and blood sugar issues or central fatty acid problems or brain inflammation issues, brain/gut access issues. You can kind of see if those symptoms apply to you and then that chapter can be very relevant. I would encourage you to check out some of those things that we have and the articles on our website, drknews.com.

Marie asks, if you think you have brain degeneration fatigue, is there anything besides movement to improve brain function?

Yes, if you have brain degeneration fatigue, you really want to immediately take an approach to save your brain because all types of brain degeneration are progressive. You really want to act as soon as possible and treating the brain is really a whole body approach. You really want to look at all the things that can impact your brain. I try to cover all of the major things, the most important things in my save your brain online program, but I also broke down each of these step by step and all the main mechanisms in my book, *Why Isn't My Brain Working*, you can get off Amazon. I have over 1,000 peer reviewed references in my brain book, so it's all about things that are in the literature and all the mechanisms and all the clinical strategies that I've been using for my practice for over 20 years that I know clinically will help you determine which pathways are involved with your brain. You definitely want to take your brain support seriously. Of course, motion and movement are important, but there's other metabolic lifestyle factors that can be a contributing factor to promoting brain degeneration.

Okay, so from Leah. Would you agree, difficulty with recovery after exercise may be connected to low glutathione, like imbalanced microbiome gut flora.

Yes, so Leah asks, would I agree if you're unable to recover after workouts that it may be related to low glutathione or imbalance in your microbiome? One of the key things to also understand is, we talked about this I think with one of our Facebook live chats on antioxidants and glutathione and one of the biggest clues that you may have, very low antioxidants which also is a big feature of the vicious cycle of chronic fatigue syndrome is when you workout, you just can't recover. The key thing when that happens is to figure out how much activity you can have where you can recover completely and do the same thing the next day. That's one of the key things to figure out your tolerance to exercise.

One of the key factors that impacts your tolerance to exercise is also your antioxidant reserves. One of the features of things like chronic fatigue is they have way more what they call pro oxidants or inflammatory mechanisms whether it's air pollution, inflammatory diets, and lack of ability to have antioxidants from eating foods that are really high in polyphenols and compounds to the point where their free radical pro inflammation is less than their anti-inflammatory system. When you exercise, you actually increase your pro oxidants during your exercise and then you'd normally have a surge of antioxidant production for many hours and hours afterwards.

But if people don't have antioxidants in their diet and they have way too much inflammation in their body to make antioxidants for, then they usually crash after workouts. Taking things like glutathione or eating a very high super food diet. Super foods, if you can Google them, they're foods that have high amounts of polyphenols and high amounts of antioxidants. They're basically you're really colorful fruits and vegetables. Beets are super foods, pomegranate is a super food, acai is a super food, berries are super foods, so those types of foods. Sometimes people are so inflamed that they have to take nutraceutical concentrates of pomegranate extract or have to take things like acetylcysteine or things like glutathione. We talked about that in one of our previous videos, if you want to check those out. Those are all part of the fatigue mechanism.

Okay Summer, thoughts on coffee, black or green tea, or caffeine for those with chronic illness. What are your thoughts on those?

What are my thoughts on caffeine, green tea, coffee, black and chronic illness? For the most part, green tea and coffee and tea, there's two components. They're rich in flavonoids, but there's also caffeine in them. Let's talk about the caffeinated teas first and coffee. The flavonoids in coffee and tea without

question have protective effects. Lots of studies have shown they support neural protection. They tend to help calm down inflammation and more and more research has come out that people that drink tea regularly and even coffee drinkers have been shown to reduce risk for things like Alzheimer's disease and neuro-inflammatory and neurodegenerative disease, so those are all beneficial.

The main issue that happens with a lot of people is, can they handle the caffeine because the caffeine is a stimulant? There's definitely some chronically sick people that would benefit from the flavonoids in tea and coffee but they can't handle the caffeine component of these drinks. They just crash. They have a little bit of tea or coffee, they crash, or they get severe anxiety that doesn't calm down for a period of time. I think each person is unique. For some people that are chronic, drinking coffee kind of really supports your anti-inflammatory system. They feel a lot better. They need a little bit stimulant to their metabolism to get them going, and it's beneficial.

For others that may have hypertension or have some adrenal inefficiencies, they can't handle that stimulant, it actually makes them much, much worse. It can go both ways. But I would definitely say, over the years I've shifted from no caffeine and no coffee and tea for chronic patients to you know what, it does offer a lot of benefits. The research shows that it does prevent a lot of different diseases. Those are all the factors involved in those drinks. Next question.

What about use of TENS muscle stimulation.

The question is the use of TENS for muscle stimulation. Technically, when you use TENS, which is electrical stimulation to a muscle, you cause that muscle to contract, you do build some mitochondria. You're only building mitochondria in one muscle group in one region, which could be effective if you have an injury and you're trying to recover and you can't move it. Using a TENS electrical stimulation, which makes the muscle contract actually does help develop some mitochondria. But when you're looking at metabolic health, you really need your entire muscular system to be involved. If you're really trying to build your energy levels, the activities you can do that involve as many muscle groups as possible would be idea. Walking would be an easy way to start.

But for some people, we have people that have had brain injuries and they can't function and they can't walk. Sometimes I'll just have them move their arms fast on their back lying down for a 30-second burst and then they stop and they do it again and they do it again. That gets their heart rate up, that changes their growth factor, it changes their opioids and they at least get muscle movement whenever they can. They can even be in bed and just bring their foot up and down as fast as they can. Whatever kind of motion they can do repeatedly until fatigue and then take a break and then do it over again, can be beneficial. For some people, that's where you have to start. Eventually, you really want them to get into motion and movement using as many muscle groups as possible. A TENS unit can be a good way to help with an injury but when you're dealing with fatigue, you really want to get as much muscle groups involved as possible.

Okay Rebecca, if fatigue from neurodegeneration sounds the same as fatigue from over stimulation with post concussion syndrome, is the chemistry the same?

Yes. The question from Rebecca is that the fatigue that happens from neurodegeneration seems like the same type of fatigue that happens post brain injury.

Yeah, post concussion.

Post concussion syndrome. Is the mechanism the same? Yes.

The chemistry.

The chemistry is the same. What happens after you get a brain injury is you get chronic inflammation in the brain and there are cells in the brain called neuroglia and these neuroglial cells get activated and they produce this inflammatory cytokine response. They do that because they have to eat up the injured protein and cells in that area. They have to get rid of that debris. They have to eat up the injured protein and cells in that area. They have to get rid of that debris. Getting rid of that debris is essential because if you don't get rid of that debris, the neurons can't fire into each other correctly. The process of a traumatic brain injury that causes inflammation in a protective way initially to get rid of the debris typically sometimes last for many, many years, which is unfortunate. These are called prime glial cells. But in that initial state, it's the inflammation from the traumatic brain injury that's uncoupling the mitochondria. The mitochondria to uncouple from the inflammation, there's very little endurance in the brain.

As the brain gets healthier and the debris gets removed, they can get some degree of recovery. For some people that have neurodegeneration, their actual brain volume has atrophied. Before you get brain atrophy, you actually get mitochondrial volume loss, you get less mitochondria in those cells. That's the earliest sign of brain degeneration. But if that cell volume is lost with mitochondria over time those actual regions in the brain degenerate, so there is definitely overlap between those. Okay, next question.

Okay Jonalyn, will taking amino acids help with stabilizing blood sugar?

Will taking amino acids help with stabilizing blood sugar? Yes, they can, especially branch chain amino acids. For some people that really have a hard time getting their blood sugar stable, they can supplement with branch chain amino acids to help keep their levels supported. It depends on what you're trying to do. Some people that have really bad blood sugar instability issues, they really may benefit from just following a ketogenic diet and getting into ketosis and shifting their energy into using ketones. That's a much more stable way of doing it. Some people that have severe blood sugar rollercoaster rides, that can be the only way they can get their blood sugar stable.

But for people that don't need to go to that extreme, taking some branch chain amino acids in between your meals, can be a good way to help keep your blood sugar stable for a short period of time until you get to your next meal. The biggest key thing is to just not miss meals and to have meals that are really high in fiber and fat where the sugar content is not overburdening the amount of fiber and fat because some people say, I had a fruit salad, there's lots of fiber in that. Yeah, but there's a lot of sugar. The balance between the sugar versus the fiber won't be enough, so they'll still crash. You really want to be vegetable dominant versus fruit dominant if you have a hypoglycemia issue but in between meals, branch chain amino acids can be supportive. Okay, next question.

Didi, how is post exercise fatigue related to mitochondrial biogenesis?

Post exercise fatigue is not related to mitochondrial biogenesis. Post exercise fatigue is related to not having enough antioxidants to quench the inflammation that's caused by exercise. If you're functioning normally when you exercise, you have during your exercise your free radicals and pro oxidants go up during your exercise and then that stops and then you get a massive production of antioxidants that quench that inflammation right after you exercise and then stay up for many, many hours throughout the day so you have this anti-inflammatory protection for your cells and your mitochondria throughout the rest of the day.

However, if you just don't have enough antioxidant substrates, you don't have enough polyphenols in your diet, you don't have enough Vitamin E or A in your diet, whatever the case may be. You don't have enough sulfur or any of the things that raise glutathione in your diet. Then when you get to that oxidative stress, even though you activate the enzymes to cause inflammation, they don't kick in, so now you have inflammation that lingers on throughout the rest of the day. Then those mitochondria get uncoupled so you can't recover, you don't feel well. What exercise, however, does is that even though it's creating this pro oxidant state, the fact that you're exercising turns on messengers. You get what they call a proteomic response, which means your cells generate proteins and those proteins generate these energy powerhouses called mitochondria, so you do develop mitochondria.

The key thing is to make sure that you have an anti-inflammatory high of polyphenol, high antioxidant diet even if you have to take nutraceuticals. At the same time, being able to exercise at an intensity and duration that allows you to do the same exercise the next day without totally crashing. Then over time, you can increase your physical demands and exercise, which will then enable more mitochondria and then you go from there.

Okay. Someone is asking you to repeat the name of your website.

The website, my website where I have all my updated information, articles, and all my programs is drknews.com, D-R-K-N-E-W-S, drknews.com.

Valerie, do you recommend NAC and glutathione or just one or the other?

Do I recommend NAC and glutathione?

Or just one or the other?

Or just one or the other. When you use glutathione as an antioxidant, the key thing with glutathione is that you have to use a liposomal form to get the best absorption. If you can get liposomal glutathione, which is typically a liquid glutathione, that's probably the best way. The cheapest and easiest way to raise glutathione is just to get acetylcysteine. Acetylcysteine is NAC. NAC is available at all health food stores, anywhere, Amazon, they all have it. Liposomal glutathione you have to do a little bit of research. For some people that have lots of inflammation, you can do both. It's a cost benefit ratio for each person, what they want to do. If you just want to implement a clinical strategy to raise your glutathione levels, inexpensively and effectively with lots of research behind it, you can take acetylcysteine, NAC anywhere between 1,500 to 3,000-4,000 milligrams a day or even twice a day if you feel like you need to.

Elaine, it seems most of the super foods are high in sugar. Should we just be looking for supplements with those nutrients or do low amounts in the diet work?

Elaine brings up a good point. A lot of these super foods are really high in sugar, so what do you do? Should you just take an extract or a nutraceutical? That is actually a good strategy that many people use. There are also things that are not high in sugar like green tea extract for example or drinking green tea that can be helpful. If you are very sensitive to sugar, then you might want to limit those. If you're at the point where you feel like you have so much inflammation and so much oxidative stress, you just may not be able to eat enough blueberries to make a difference for you. You may actually need to get pomegranate extract and blueberry extract as supplements you can find in a health food store or take high amounts of antioxidants like acetylcysteine for example or glutathione to really support your mitochondria.

Sean says, this is really helpful, thank you. This should be a book.

There's like 20 books we have in mind, we're just barely hanging in there functioning, but thank you.

Deborah, is there any connection between low blood pressure and fatigue or brain degeneration and other issues?

Yes. The question from Deborah, is there a connection between low blood pressure and fatigue and brain degeneration?

And other issues.

And other issues. Yes. I talk about this actually in my book extensively and in our online program, the Save Your Brain program. But low pressure and we say low pressure, normal blood pressure is 120/80. If your first number, systolic number is below 100, that's not good. If your diastolic number, the second number is 80 but it's like in the 60s or very low 70s, that's not ideal. For example, if someone has a blood pressure of 90/60 and they're hypotensive, that could cause some problems. Now, many people in healthcare, a lot of doctors in healthcare go, that's great because your low blood pressure is not high and that's true to some extent because the major concern for high blood pressure is that it is an absolutely serious risk factor for stroke and damage to the arteries and cardiovascular disease. I don't think that's even controversial. That's pretty much a well-established mechanism.

But low blood pressure, people who have low blood pressure they end up having more chronic diseases, more fatigue issues, more energy issues, they die sooner, so there's lots of health problems associated with low blood pressure, it's just not emphasized. What happens with low blood pressure is you also get something called low perfusion and perfusion is your ability to push blood into your cells. When you have low blood pressure, you have less perfusion. That's why when you have low blood pressure, you have really cold hands, really cold feet, really white nail beds. This inability to push into the tissues is a problem because the blood is carrying all the nutrients that you take as a nutritional supplement or through your diet, it's carrying oxygen and glucose that your mitochondria need for function. When you have someone who has very low blood pressure, they also have very low perfusion. It's really hard to get oxygen and glucose and nutrients to the mitochondria and different tissues in the body, for example the brain.

Your brain is your most distal and vertical structure. It really depends on perfusion to be able to get your blood from your heart to your brain. People with low blood pressure typically have many issues of brain fatigue and energy and their mitochondria is not working well because of that. In previous videos, we really talk about strategy to support that and in my book I talk about strategies to support that, but sometimes it's eating more salt in your diet. Taking things like licorice root can help raise your blood pressure, and that's important to do.

Okay. Lana was asking, is it possible to raise blood pressure, she has Hashimoto's and cold feet.

By the way, low blood pressure as a clinician, is one of the most overlooked mechanisms that cause significant chronic symptoms of endurance issues, fatigue, and may contribute to neurodegeneration. There are now studies in the literature that have linked hypotension, low blood pressure, to promotion of neurodegeneration as well, which is interesting to see that it's coming out in the literature more and more.

Steph asks, how do you test or know the mito, I think she means mitochondria, are getting the oxygen then need. How do you test for that?

There is no laboratory test to know if the mitochondria are getting necessarily the energy they need. Listen, as soon as you hit the right pathway, it's noticeable. People's energy levels change dramatically once you uncover things that are uncoupling the mitochondria and improve energy levels. Yeah, sometimes uncoupling mitochondria could be someone is sensitive to egg protein. They get off egg, their inflammation dramatically goes down and their energy levels boost up. That's a mechanism where the inflammation was uncoupling the mitochondria. For other people, they'll have to break the vicious cycle of being sedentary and getting motion and movement to finally start to get a boost in energy and they look back like a month ago and think about wow, I couldn't even walk around and do any kind of exercise. Now, I'm able to do stuff. Those are all noticeable. You're going to see very clear noticeable symptom and function change. The key thing is probably function change to realize that these things are working but there's no lab test to determine if oxygen is getting into your mitochondria from a basic bio burner.

Okay. Jacqueline, is there any research looking at timing of antioxidant supplementation in relation to exercise to prevent PEM.

The question is when you should take antioxidants ...

Any research looking at the timing.

The timing of taking antioxidant supplements after you exercise?

In relation to exercise to prevent PEM.

To prevent post exercise malaise or I don't know.

I don't know what PEM is.

Yes, there are studies that have linked when you should take antioxidants after you exercise to have the reduced effect on oxidative stress from exercise. There are various outcomes out there but for the most common overlap between these studies is really in that half hour to hour-and-a-half window right after exercise, that's the benefit of taking some antioxidants. That would be a good time to take a high energy drink or take some antioxidants or bio flavonoids if you're trying to avoid that exercise crash. For people that really have a hard time of falling apart when they exercise, it wouldn't be a bad idea a half an hour before to take some antioxidants or things like pomegranate extract or whatever type of antioxidant you use like an acetylcysteine and then exercise and then be able to take some afterwards.

You've got to be careful though before exercise. If you take capsules, you might get really nauseous and sick, so you may want to use a liquid form of supplements to really help if you're going to do it right before exercise. I like to use a liquid resveratrol or a liquid turmeric before exercise. That seems to be very useful.

Okay. This is just funny. People are commenting on "great new mic."

Yes, thank you for the great new mic. This was actually always here before, but now I just raised it. Thank you for the comments.

It's just funny. It makes me laugh. **Lillian, would you suggest turmeric, ginger, and licorices for low blood pressure and better circulation and/or CoQ10 for energy.**

Okay, would I suggest turmeric, licorice and what?

Turmeric, ginger, licorices.

Turmeric and ginger are not going to have the biggest impact on your blood pressure. They're going to have an antioxidant effect, which is great. Licorice root is going to be the one that really impact blood pressure because it modulates an enzyme that allows you to activate aldosterone and helps you with sodium retention. If you're really trying to take a botanical for increasing blood pressure, it's really going to be the licorice, not so much the turmeric and ginger. Then the second part of that question was?

And CoQ10.

CoQ10 is the most popular supplement for supporting the mitochondria. You could definitely try it. The problem with the CoQ10 is it's expensive and for most people taking CoQ10 doesn't really change your energy levels. Obviously, if you take certain things that deplete CoQ10, the most common cause is taking a statin medication. Statin medications deplete CoQ10. It absolutely should be supplemented if you take any kind of statin, to take some CoQ10 to counteract the depletion. But in a real clinical setting versus the world of nutrition on the internet, in a really clinical setting, you don't get much change in energy until you find the mechanisms that are uncoupling in the mitochondria or causing inability to deliver fuel or oxygen to the mitochondria. Things we talked about like getting the brain healthier, stabilizing blood sugar levels, calming down your immune system, finding inflammatory triggers. Those are all the key things.

If you're going online, trying to read articles about what supplement to take for your fatigue, you will be spending a lot of time energy, and money. You've got to move. You've got to get motion activity. You've got to find the underlying causes and you've got to remove triggers and you've got to stabilize your blood sugar. That's where you want to invest your time and energy in by the way instead of just trying to find the next new supplement.

Okay. Sean asks, are you concerned with NAC causing intestinal permeability, sorry, since it decreases mucous in the intestines? Many papers on Pub Med suggest long-term use as detrimental.

Yeah, these papers on NAC causing gut issues are over exaggerated. I have no issues with using NAC to support the gut long-term even for myself or for my patients. A lot of times you find one little mechanism with NAC but there's no study that shows NAC causes intestinal permeability, it's just one pathway is impacted that produces mucous. But the antioxidant, the anti-inflammatory effect is much more impactful in the big picture. There's also several studies that show the gut barrier doesn't break down until glutathione levels get depleted. The blood/brain barrier doesn't break down until glutathione gets depleted and the lung barrier doesn't break down until glutathione gets depleted and NAC raises glutathione.

This is where, unfortunately on the internet and in social media, there's people that immediately want to get the shock effect, so they pull out one piece of the research paper and then they make this big deal about it, which is actually the exact thing you shouldn't do with research, and then they create this buzz and then everyone freaks out about things like that. NAC in the gut is one of them. I would say don't worry about NAC and kind of gut permeability issues. It's one of the most useful things you can do to keep your gut healthy.

Okay. Sean again, do you find that circadian rhythm dysfunction a major contributor to chronic fatigue?

Yes.

You have not really discussed it. I'm very interested to know your perspective. Thank you.

Yes, so Sean, I didn't get a chance to cover a lot of things related to chronic fatigue because of limitations of Facebook Live posts. But you do bring up a good point, which is the circadian rhythm. The circadian rhythm is part of the aspect of fatigue related to healthy sleep. Your circadian rhythms have to be functioning ideally to have energy production as well. Your cortisol levels are high in the morning. They should go down by the time you go to bed and then when you sleep, your cortisol levels should eventually go back up and you should have cortisol levels spike in the morning so that it actually wakes you up normally and that's a normal response.

In between this cortisol, circadian rhythm going up high in the morning and then down at night and then going back up in the morning, there's an inverse relationship with melatonin that's also happening. Your melatonin levels are low in the morning and at nighttime they get high as your cortisol levels go down. These things have dramatic impacts on your metabolism and your energy function and fuel delivery and energy storage throughout the day. If you're constantly sleeping at different times throughout the day or switching your circadian rhythms, it's really going to mess up your circadian rhythm and your health and your energy production as well. Another key thing to add is making sure you sleep and wake up in a routine structure each night is really, really important for your overall health and for your energy production.

Okay, can you let people know we're not avoiding their questions. It's just this thing goes so fast.

You guys, we're really not trying to avoid your questions. We're doing the best we can. We're two people with bad eyesight trying to read questions.

Hey.

You have glasses on. We're trying to read them and trying to answer the best we can. Please don't take anything personal. I'm trying to schedule an hour of my day each week to do these, to get information out there. If we don't get to your question, I do apologize. I think we can take one last question here.

Okay. Nancy, she wanted to know if you're avoiding her question. [crosstalk 00:59:41]. With inflammation of the brain and spinal cord possible a virus with enhanced neurotrophic ...

Okay, Nancy. If you have myalgic encephalomyelitis, if you have a neural inflammatory impact on your nervous system, you're going to have fatigue because that's a chronic inflammatory condition. At the end of the day, unless you figure out how to calm down that inflammatory reaction with whatever the appropriate clinical strategy is, you're going to have chronic fatigue. Any kind of chronic inflammatory condition whether it's inflammatory bowel disease, whether it's an environmental-induced asthma, like air pollution causes asthma, whether it's multiple food reactivities, whether you have celiac disease and you keep eating gluten and that causes inflammation that gets you tired, unless you stop those mechanisms, you're not going to change your energy levels because the chronic inflammatory response is going to uncouple the mitochondria. That's really the key thing there.

Let me just summarize the key concepts and then hopefully, there's some useful information from this talk to help find your way and navigate your way through fatigue. Ultimately, when you look at fatigue, fatigue is this balance between how much mitochondria you make, which is called mitochondrial biogenesis, so that's related to how much activation your muscles get, your body moves, your brain gets activated, those are all important to actually make mitochondria. That mitochondrial biogenesis has to happen from activation and use. A sedentary lifestyle, you stop using your brain, stop doing activities is

a very quick way to increase the percentage of mitochondrial loss you'll have each decade as time goes on, so you really want to be active and do things as much as possible.

Then you have factors that these mitochondria that produce energy through the production of ATP through all your cells they need glucose, so you have to have blood sugar stability. They need oxygen, you need to have healthy amounts of circulation and blood flow and things like inflammation uncouple them. You've got to find inflammatory triggers and try to remove them. At the end of the day, you're trying to make the biggest difference. The biggest mistake most people have with chronic fatigue is they don't get motion and movement and activity, so that they can't get mitochondrial biogenesis. The second biggest one is that they have blood sugar instability issues.

Anyways, I hope the information represented helps and we'll put together a new topic for next week. Thank you all for-

Okay, hold on really fast. Sorry, I'm so sorry. Susan asked for this, there are so many great questions each week that go unanswered. Is there any way we can get replies afterwards, not live?

Susan asked, there's lots of great questions that get answered each week, how do we get replies afterwards? No, there's no other way right now. You guys, I'm still trying to publish research, I'm still working, I still have a practice, I still have a family. You can literally live your entire life on social media if you have the time but we're getting some great research published that I think is going to have an impact. I have a full-time job and practice, I'm an educator, I teach healthcare professionals, I have seminars and material to teach them with, so this is the best I can do with answering questions for now. But thank you all for joining us and I really appreciate it. I hope you're all healthy and thank you for joining us.

Copyright 2020, Datis Kharrazian