# The Benefits of Intermittent Hypoxic Training for Optimizing Mitochondrial Function
# A Special Interview With Dr. Arkadi Prokopov
## By Dr. Joseph Mercola

**Dr. Joseph Mercola:**

Welcome, everyone. Dr. Mercola helping you take control of your health. And today, we are joined by Dr. Ark Prokop, who is, obviously as you will tell in a moment, has a very thick Russian accent and he's from Russia. It's a country that has been exploring a lot of radical innovations that we have not dived deeply into in the United States, and he's going to share some of those insights with him today. I'm particularly fascinated in understanding his perception of mitochondrial function because that is, without any question or doubt, one of the single most important strategies you can do to optimize your cellular energy. It's the core of almost everything that you do to improve your health is mitochondrial function. So, anything that addresses and improves that is an interest of mine. So, that's one of the reasons why I invited you here today. So, welcome and thank you for joining us.

**Dr. Arkadi Prokopov:**

First of all, thank you very much for [the] invitation. I must say that I'm your follower since 2001.

**Dr. Joseph Mercola:**

Wow. That's 23 years, 23 years.

**Dr. Arkadi Prokopov:**

Exactly. I was working in New York City, and I found out that your broadcasts and your books are very, very motivating, interesting, and since then I'm following you.

**Dr. Joseph Mercola:**

Oh, good. Well, you're a wise man and hopefully you can share some of your wisdom with me.

**Dr. Arkadi Prokopov**:

Yeah, I hope. I hope.

**Dr. Joseph Mercola:**

Yeah, so why don't you first start by giving us a little bit of background for your history? Because clearly, you've been trained in Russia and have acquired some significant expertise. So, I'd like to know if you can share that with us now.

**Dr. Arkadi Prokopov:**

Yes, I graduated from Moscow Medical University in 1980. And I worked about one year in emergency as [an] emergency doctor, but my interest was always in the biomedical research, specifically research with professional divers. So, I entered my postgraduate studies, and I was doing my dissertation on the topic of improvement of stress resistance in divers. And it was very interesting because all [the] people who were involved, they should first of all do experimentation on themselves. So, we first graduated as divers, professional divers, and then conducted a lot of experiments in Barlow chamber and also in open water and so on. And that was-

**Dr. Joseph Mercola:**

Excuse me for a moment, but wouldn't diving be a simulation of hyperbaric therapy?

**Dr. Arkadi Prokopov:**

Yes, of course. In many aspects, diving is actually a kind of simulation of hyperbaric treatment. And moreover, we use Barlow chambers, hyperbaric oxygenation, for many conditions associated with diving trauma, like bends and barotrauma and so on. So, I was working 10 years in this research, but then the situation changed in Russia and these studies were cut significantly and I just returned back to medical practice. And what I learned during this studying of physiology of diving and the stress resistance of divers, it helped immensely by application of this knowledge to a lot of various diseases, such as asthma, hypertension, chronic inflammation and some chronic infections. And I was always interested [in] what is the best application of oxygen treatment to stimulate nonspecific stress resistance. And from many, many studies, it became clear, paradoxically, that the most efficient intervention is intermittent hypoxic treatment. So, since 1994, I was working in Germany, first in a private practice-

**Dr. Joseph Mercola:**

But before we go there, I think it might be wise to explore what is intermittent hypoxic therapy? I know what it is, but I think if you can explain that and then also the origins of its history. Where did it start from? Was it in Russia?

**Dr. Arkadi Prokopov:**

Yeah, actually, [the] scientific application of intermittent hypoxic treatment started in Russia, at the end of '70s. Because paradoxically, it was found that intermittent-controlled normobaric hypoxia is much more efficient than continuous hypoxia, such as, for instance, in hyperbaric chambers or in the mountains. This discovery was made by Professor Chirov. He studied hypoxic treatment in various applications.

First of all, as a radioprotective treatment because during radiation, if you reduce partial pressure for oxygen, we will see then a significant protective effect on healthy tissues. Tumor tissues are not protected because they're already hypoxic and they don't feel this small decrease of oxygen partial pressure. But for healthy tissues, it's a huge difference. And then he found out that intermittent hypoxia is taking place during embryonic development. So, in [the] uterus and even before fertilization, there are significant changes, variations of partial pressure of oxygen,

oscillations or forks in the uterus. And it was not clear what is the physiological purpose of these oscillations.

And now, decades later, we understand that this is a powerful mechanism to control [the] quality of mitochondria. And intermittent hypoxia is very often in nature. For instance, when we have some physical activity, when we stress our muscles when they are contracted, the circulation is blocked and [the] muscles experience some kind of hypoxia. Then during relaxation, blood delivery is again open and muscles become again oxygen and nutrients. And this is the universal mechanism, which is providing continuous repair recovery of the mitochondria and other cellular structures. So, why not use this natural mechanism to apply it for other purposes, like [the] enhancement of endurance in athletes? And now, it is very well-known as altitude training. Thousands and thousands of athletes use altitude training to stimulate recovery, to stimulate functionality, and it has a lot of applications.

**Dr. Joseph Mercola:**

So, can you tell us how it was implemented initially in the '70s in Russia? And then what the most current applications are now and basically how it's utilized? The mechanics of it, what it looks like.

**Dr. Arkadi Prokopov:**

Yeah. Because, you know, at the very simple way it can be simulated without any devices. Just by holding your breath intermittently – For instance, now it's [a] very well[-known] method by Wim Hof, who recovered the very old variant of pranayama breathing, [the] so called initial sri chakra pranayama, so it is called. Everybody knows what is Wim Hof breathing. But we can do the same without [the] stress of hyperventilation, without reducing carbon dioxide, just providing intermittent flow of oxygen-depleted air into the mask. [The] patient [is] just using the face mask and the device delivers intermittently hypoxic air with controlled amounts of oxygen and room air or even hyperoxic air. So, now we have the fourth generation of such machines. They're called hypoxicators. They have biofeedback, they are computer-controlled, and they allow [to] perform all kinds of treatments, all kinds of protocols.

**Dr. Joseph Mercola:**

Yeah, I've got one of those units. I've had it for about a year. And it's essentially a cube, maybe 2 1/2-foot cube, maybe 3-foot, somewhere around that, probably 2 1/2 feet [or] 30 inches, and essentially delivers, as you said, this combination of hypoxic [air]. And the amount of oxygen in the atmosphere at sea level is close to 20% and-

**Dr. Arkadi Prokopov**:

Yeah, 21%, so above.

**Dr. Joseph Mercola:**

Yeah, so 21%. It modulates it down to therapeutic levels, which seems to start about 14%, and can go down even to 10%, or even a little bit lower. That's the dangerous level. And you stay

there for a few minutes, maybe even up to seven, eight or nine, 10 minutes, and then you adjust to that and you get this hyperoxic error. So, in the case of my unit, it goes up to 34% oxygen, and then that's only for a minute or two, and then you cycle back and forth.

**Dr. Arkadi Prokopov**:

Exactly.

**Dr. Joseph Mercola:**

And then it's an interesting experience because you can't do much in that environment. So typically, what you do, or at least what I've done is listen to sound, music. I mean, you can listen to podcasts but I don't think it's a good idea. So, you listen to music and you go into meditation.

**Dr. Arkadi Prokopov**:

Exactly.

**Dr. Joseph Mercola:**

Yeah, that gives you better benefits. So, I'm intrigued with it. And I didn't – There's not a lot of research on this. Well, maybe there's a lot of research. Not a lot of written that's available in PubMed, that's for sure. I couldn't find it. And maybe I just didn't know what to search for. But I'm curious as to – one of the reasons I invited you is to help me understand how this is working. I know it works. There's no question. My conclusion – This is my thesis and I see how it integrates with your answer is that a big part of it is it lowers your CO2 (carbon dioxide) levels. And I understand that your oxygen comes up afterwards. But when you lower your – I'm sorry, it increases your CO2 levels because you're in hypoxic air so that you don't get respiratory alkalosis, you get respiratory acidosis because your CO2 levels go up. But when your CO2 levels go up, it increases the oxygen circulation to your body even though you're breathing hypoxic air. That's a normal response. So, is that part of the mechanism?

**Dr. Arkadi Prokopov:**

Yes, partially, it is, it is. But normally, when you're getting into [an] hypoxic environment, your breathing increases. In altitude, it induces hyperventilation and hypocapnia. When you do this breathing with normobaric air through the mask or as you did in a cubicle – I must say, just that in the cubicle, it's not that efficient as using simply a mask because the volume which you get in the mask is much more physiologically relevant and you get much faster oscillations. The effect of meditation increases the – partially it is because the plate of the capillaries, exactly. In hypoxia, capillaries became wider. In our brain, for instance, hypoxia increases perfusion of the blood up to 40%, in just the hypoxic response. And CO2 plays a significant role if it's – for instance, many people live continuously in subclinical hyperventilation. So, they have much lower CO2 as it's better for the mitochondria.

**Dr. Joseph Mercola:**

Another term for that would be overbreathing.

**Dr. Arkadi Prokopov:**

Overbreathing. Exactly.

**Dr. Joseph Mercola:**

When you breathe too deeply, typically. If you breathe faster [too], but mostly it's the depth of your breathing that causes you to expel too much CO2 and you get to really low CO2 levels, and that is dangerous. That is really dangerous.

**Dr. Arkadi Prokopov:**

Absolutely. Especially when it's chronic overbreathing. And because now people live in continuous stress, this overbreathing establishes automatically.

**Dr. Joseph Mercola:**

It is a psychological habit that is really difficult to overcome. I just interviewed Dr. Peter Litchfield on this. I don't know if you're familiar with Dr. Litchfield's work but he's one of the experts in the world that [are] addressing the behavioral overbreathing habits with psychological behavior modification.

**Dr. Arkadi Prokopov:**

Yes, I do agree. But I wouldn't say that this psychological component is very significant because-

**Dr. Joseph Mercola:**

He would disagree with that.

**Dr. Arkadi Prokopov:**

Of course, yeah, we should discuss these different opinions and ideas. Because as soon as people improve [the] quality of their mitochondria, they stop overbreathing.

**Dr. Joseph Mercola:**

Really? So, that's been your experience? That's been your experience?

**Dr. Arkadi Prokopov:**

Absolutely. Because where do we get carbon dioxide? We produce [it] from [the] mitochondria. It's an element metabolite. And if the mitochondria are not active enough, if they are just lazy for different reasons, they just don't produce enough carbon dioxide. And then hyperventilation during stress even further reduces carbon dioxide, and then we get in this vicious circle. So, there are two ways you can increase the amount of carbon dioxide by very simple means, like breathing in a bag, breathing in adjusted controlled volume or even simpler, we just increase physiological dead space. So, you increase [the] volume of the air, which is pendling in your trachea. If you use [a] mask and the tube, then you increase this air which is pendling. By this

way, you immediately increase partial pressure of CO2, and it reduces many symptoms of overbreathing in minutes.

**Dr. Joseph Mercola:**

Yeah, it's kind of like breathing into a paper bag of some sort, just [inaudible 00:16:27] paper bag.

**Dr. Arkadi Prokopov:**

Yeah. But you know, this kind of devices, they're called hypercapnicators. And there are hundreds, virtually hundreds of them patented, and they were produced. Now we have in Russia two or three variants of these hypercapnicators.

**Dr. Joseph Mercola:**

Yeah.

**Dr. Arkadi Prokopov:**

But nevertheless, it's just a symptomatic treatment.

**Dr. Joseph Mercola:**

Right.

**Dr. Arkadi Prokopov:**

Because as soon as you stop it-

**Dr. Joseph Mercola:**

It's gone.

**Dr. Arkadi Prokopov:**

Overbreathing again, and you have the same problems. The other way, if you regenerate your mitochondria, if you make them work more efficiently [and] economically, it produces a much better level of endogenous carbon dioxide. It resets the capnometer, which we have in our brain, we have in our arteries. We have thermostat and we have also capnostat. Because normal partial pressure of carbon dioxide is from 35 to 45, but most people are lower than 35. So, if [the] mitochondria [are] functioning optimally, it automatically levels up the capnostat and we see a reduction and complete elimination of all problems connected to overbreathing.

**Dr. Joseph Mercola:**

That's interesting. So, I wonder if you have – I want to now dive deep into what you're perceiving as an optimal intervention to improve mitochondrial function. I've said some theories and perceptions on that too, and I'd like to discuss with you, but before we go there, have you ever played with or explored the use of exogenous CO2 therapy? So, rather than allowing your

body to rebreathe and increase the CO2 that way, but actually administering CO2 as a therapeutic intervention.

**Dr. Arkadi Prokopov:**

Yes, of course. Yes, of course. First of all, when you stay in a diving chamber, a hyperbaric chamber, there is automatic control of CO2 level, and there are CO2 scrubbers to keep it [at] an optimal level. So, I was engaged in this research. Moreover-

**Dr. Joseph Mercola:**

How high did the CO2 go in those chambers? What percent? Because normally, it's half of 1%, right?

**Dr. Arkadi Prokopov:**

Yeah.

**Dr. Joseph Mercola:**

Or I don't know, is it 10-

**Dr. Arkadi Prokopov:**

It's 0.3, 0.3. So, about this. 0.5, 0.6, it's already sensible, people already feel it. If you have this high level for a long time for a continuous time, it actually makes some problems, because it makes headache, it produces discomfort. So, the-

**Dr. Joseph Mercola:**

Excuse me for a moment, but I thought that a common cause of headaches was vasoconstriction, especially for vascular headaches. The blood vessels in the brain become really tight, and they squeeze in the brain. Even though the brain doesn't have sensors, it's a pressure problem that causes some discomfort.

**Dr. Arkadi Prokopov:**

Yeah, I agree.

**Dr. Joseph Mercola:**

And then the CO2, when you increase it, that's a magnificent vasodilator and it relaxes those blood vessels and the headache disappears.

**Dr. Arkadi Prokopov:**

Now, we make a step in[to] a very serious problem of [the] glymphatic system in our brain.

**Dr. Joseph Mercola:**

Okay.

**Dr. Arkadi Prokopov:**

You know the glymphatic-

**Dr. Joseph Mercola:**

I'm sorry, because of the accent, it's hard to say. Is it lymphatic or glymphatic?

**Dr. Arkadi Prokopov:**

Glymphatic.

**Dr. Joseph Mercola:**

With the "g"? With the "g"?

**Dr. Arkadi Prokopov:**

Yes, with "g." Because in our brain, we have very limited drainage of the metabolics. And the glymphatic system was discovered I would say maybe five years ago. It's a system which provides circulation of cerebrospinal fluid. And actually, the removal of metabolites runs through [the] glymphatic system. And [the] glymphatic system is very sensitive to the changing blood pressure and blood volume because our skull is not flexible. For instance, if [the] delivery of blood increases, but simultaneously the release of blood is not released, then we have this difference in pressure and we can feel headache. And the glymphatic system is providing this drainage of glymphatic cerebrospinal fluid, and it is very much controlled by intermittent hypoxia.

Because that feeling of meditation that you had when you were in this oscillating atmosphere, it is caused by small changes of volume in the brain, arteries, veins and glymphatic system. Glymphatic system starts to pump much better during these oscillations, and it clears metabolites from the brain much faster. And therefore, we will see, very practically, instant relief of some headaches during hypoxic treatment [and] reduction of blood pressure. And this meditative state, it develops during the change from hypoxia to hyperoxia because of the improved drainage function of [the] glymphatic system. This is at least how I can explain what I see with my patients, and of course, I do it with myself.

**Dr. Joseph Mercola:**

Interesting. So, maybe we can dive into the recommendations you have to optimize mitochondrial function. But before we do that, I can share what I perceive as a useful strategy. Because you are correct. Virtually all the CO2 in the body is produced in the mitochondria electron transport chain when you're able, ideally, to metabolize carbohydrates, specifically glucose, which breaks down – I mean, glucose and fat both break down acetyl-CoA, but the process of converting fat to supply the acetyl-CoA to the mitochondria is problematic, largely because of the way that electrons are shuttled around. And you actually produce mitochondrial efficiency by 25% to 50% when you're metabolizing fat, and you do that when you're fasting or even intermittent fasting, or just have a high-fat diet. So, that's a potential problem. And you're not going to get maximum CO2 production because the fuel that optimizes CO2 production is glucose. No question about it, that is the king of the fuels. And you're going to not only increase

CO2 production, you're [also] going to increase metabolic water – structured water, sometimes called, deuterium-depleted water otherwise known as – and you will also increase ATP (adenosine triphosphate) production by 25% to 30%, and you reduce reactive oxygen species, which is another issue to be concerned about with longevity. If you have too much oxidative damage, you got a problem. And you reduce something called reductive stress, which contributes to the oxidative damage. So, that was a mouthful. I wonder if you can comment on that and help me understand how that integrates into your view of mitochondrial function.

**Dr. Arkadi Prokopov:**

First of all, I must say that if you don't load your mitochondria continuously, they automatically degrade from just from misuse.

**Dr. Joseph Mercola:**

What do you mean by load?

**Dr. Arkadi Prokopov:**

The mitochondria can feel only two interventions, two inputs: what fuel you deliver to them and what amount of oxygen you deliver to [the] mitochondria. If there is a continuous flow of fuel, nutrients, and [a] continuous, stable level of oxygen, the mitochondria undergo degradation because during this ad libitum nutrition and ad libitum oxygen, still oxidative damage in mitochondrial DNA results in a growing population of damaged mutated mitochondria.

**Dr. Joseph Mercola:**

Interesting.

**Dr. Arkadi Prokopov:**

And mutated mitochondria have smaller DNA molecules. The normal DNA molecule [of] the mitochondria [is] 16.5 kilobase and it's, let's say, like this. But normal metabolism results in a continuous mutation and it makes the mitochondrial DNA smaller because mutations [were] repaired very insufficiently. Just a piece of mutated, circular DNA will be cut off and the ends will be glued together.

Next step, next step, in a stable situation, what molecules will reproduce faster? The smaller. The smaller molecules make their copies a little bit faster than the larger. Therefore, if everything is stable, normal, very comfortable, the mutated, disadvantageous mitochondrial DNA will dominate and we see it with [the] normal aging process. We see it in some diseases also when [there's] accumulation of mitochondrial mutation, especially in neurodegenerative diseases. So, the task is to continuously eliminate or help [the] natural process of elimination of mutated mitochondria. This process is taking place normally. It is mitophagy. But mitophagy is also not getting better with growing age. It also can be reduced or slowed down with many mitochondrial toxins and of course with infection.

Therefore, if we just help this process, this natural process of mitochondrial regeneration, we prevent accelerated decline of mitochondrial quality. And the best tool for this is intermittent

hypoxic training. Because when we introduce intermittent hypoxia to the populations of different – in the cell, we have two populations of mitochondria. One, [the] original, wild type mitochondria, they're okay, they're perfect. But the growing population of mutated mitochondria, they are much more sensitive to oscillations. They don't have enough protective mechanisms. Because, you know, mitochondrial DNA protects itself. There are a lot of antioxidative enzymes like superoxide dismutase, catalase peroxidase. But mutated mitochondria don't have enough of these enzymes, so they are just killed by oxygen oscillations.

**Dr. Joseph Mercola:**

Does mitochondrial DNA have histones?

**Dr. Arkadi Prokopov:**

No. As far as I know-

**Dr. Joseph Mercola:**

They don't? It's only nuclear?

**Dr. Arkadi Prokopov:**

It's naked. It lays naked in the stove, in a very hot stove. You know the [crosstalk 00:28:59]-

**Dr. Joseph Mercola:**

Yeah, yeah. The oxidative stress, that's where most [crosstalk 00:29:02]-

**Dr. Arkadi Prokopov:**

Oxidative stress, and also very high temperature.

**Dr. Joseph Mercola:**

Oh really?

**Dr. Arkadi Prokopov:**

It is shown now that [the] temperature [of] functioning mitochondria is about 15 degrees Celsius higher than the environment, its temperature.

**Dr. Joseph Mercola:**

Wow, I never heard that before. That's amazing.

**Dr. Arkadi Prokopov:**

Oh, it's [in] publication since 2020.

**Dr. Joseph Mercola:**

I'm not denying it, I just never heard of it. That's amazing.

**Dr. Arkadi Prokopov:**

That tells a lot about the stress, which the mitochondria endure.

**Dr. Joseph Mercola:**

Yeah, yeah. So, they truly are furnaces.

**Dr. Arkadi Prokopov:**

Yes, they are furnaces.

**Dr. Joseph Mercola:**

They truly are. Yeah. Wow. Biological furnaces. I never knew that.

**Dr. Arkadi Prokopov:**

Absolutely, yeah.

**Dr. Joseph Mercola:**

So, let me go back to – you said there are two strategies to optimize mitochondrial function. One is to – And they're both the same process. Essentially, you need to throttle the fuel up and down. Continuous fuel is a disaster. So, continuous oxygen, the same level. Continuous food, the same level. So, let's go with the food first. So, this would support the administration of intermittent fasting where you're not eating fuel for maybe the majority of the day. Maybe eight hours a day, maybe 10 hours a day you're eating and the rest you're not eating. Is that a strategy that you perceive as optimal from the fuel perspective to address this issue?

**Dr. Arkadi Prokopov:**

Absolutely. What I see – And not me, it's a lot of research and experience on the clinical field, that on the fasting state when your ketone metabolism is much higher, the mitochondrial energy production is more optimal. When the mitochondria are healthy, when we have [a] healthy mitochondrial population. But when the mitochondrial population is a mix of mutated and healthy mitochondria, that can cause problems. Therefore, many people cannot start fasting, they cannot start intermittent fasting or ketogenic diet, because their, let's say, 50% mitochondria are dysfunctional.

**Dr. Joseph Mercola:**

Oh, okay.

**Dr. Arkadi Prokopov:**

As soon as we repair mitochondria with gradually introducing intermittent fasting, gradually introducing ketones, and in parallel, intermittent hypoxic training, we see immense improvement of energy metabolism, we see improvement of OXPHOS (oxidative phosphorylation) and ATP production, and interesting, most interesting, much more economical. So, [the] mitochondria, in idling state, they consume much less oxygen as an average human being. On the other hand, at

the physical load or functional load, they're much more efficient. So, we're optimizing mitochondria, we're improving [the] quality of mitochondria.

**Dr. Joseph Mercola:**

Okay. So, I'm assuming you're doing this in your lab, is that correct?

**Dr. Arkadi Prokopov:**

I do it, let's say, the last 40 years of my life, [inaudible 00:32:19]-

**Dr. Joseph Mercola:**

Okay. I'm really intrigued, because the big question on the table is how – and I don't know that this is really well done outside of the research lab, where they had assays like the seahorse assay. How do you assay mitochondrial function? There is no simple test to see how well-

**Dr. Arkadi Prokopov:**

Absolutely. It's very difficult. It's really challenging on the lab level because we see very much discrepancy between clinical results and what we see in the labs. In Germany where I work, the last time I worked in Germany also, we have very good labs for mitochondrial diagnostic, like ArminLabs and [inaudible 00:33:03], and they have mitochondrial energy tests. So, it shows the mitochondrial quality. You take just blood and they separate leukocytes, and then from leukocytes, they extract mitochondria.

**Dr. Joseph Mercola:**

Yeah. Let me just [inaudible 00:33:22], your pronunciation makes it somewhat hard. It's leukocytes in typical English.

**Dr. Arkadi Prokopov:**

Leukocytes, yeah. White blood cells, white blood cells. And we see that really – for instance, with myalgic encephalomyelitis, that's chronic fatigue syndrome, we see that there is a positive correlation. Most patients show very low mitochondrial energy production. They show increased proton leak-

**Dr. Joseph Mercola:**

Okay, so it's very clear the information you're sharing is valid because you're one of the few researchers that has access to these tools to measure mitochondrial function. I wish to God it was a commercial availability. We could advance medicine so much more quickly, because that's the best tool to measure how healthy you are, is you're measuring assay and your mitochondrial function. There are no good commercial assays for it. They just don't exist.

**Dr. Arkadi Prokopov:**

You know, that was a good news. But the bad news is that we don't always really see a serious correlation, because we see sometimes that mitochondrial energy analysis shows there is

improvement but we see no clinical improvement. And the reverse. And the reverse also. We see a drastic clinical improvement, but very very low on mitochondrial [energy analysis]. And it can't be explained.

It's not something – it can't be explained because mitochondrial populations are heterogeneous. They are very different. What we see in the blood, in white blood cells, it comes from bone marrow. And the clinical symptoms, we get from neurons, from muscles, from liver. And there are different populations of mitochondria, and what is going on in the brain we don't see immediately in the white blood cells.

**Dr. Joseph Mercola:**

Yeah, it makes perfect sense. So, most of the mitochondrial assays are using white blood cells to measure?

**Dr. Arkadi Prokopov:**

This is the standard lab test by ArminLabs. I can send you just the links. I think they have also patients from [the] United Kingdom, from the United States. So, there's no problem. Therefore, the most relevant mitochondrial tests to my experience are very simple clinical tests.

**Dr. Joseph Mercola:**

Okay, what are they? Enlighten us.

**Dr. Arkadi Prokopov:**

Basically, the level of lactate in the blood.

**Dr. Joseph Mercola:**

Oh, blood lactate levels?

**Dr. Arkadi Prokopov:**

Of course, blood lactate, because the more lactate the patient has, it normally correlates with, for instance, chronic fatigue syndrome. It shows systemic mitochondrial dysfunction.

**Dr. Joseph Mercola:**

Yeah, yeah, yeah. It correlates.

**Dr. Arkadi Prokopov:**

Then there are functional clinical tests, just physiological tests. For instance, for healthy people, this can be VO2 max (maximal oxygen consumption), VO2 max, which can be done very simply even [in] at-home setting with a stationary bike, or treadmill, or running 12 minutes, like [the] Cooper test. And you can correlate it with VO2 max, the correlation is very high.

**Dr. Joseph Mercola:**

So, let me discuss that because I think the lactate might be better, and I'll tell you why. I was a runner for almost 45 years, over four decades, because I started very early in my life and I quit like 15 years ago. And I got to be pretty good with respect to endurance training. And I know there's an adaptive phase. And when you first start, you're not that good. It doesn't mean you're not healthy, it's just [that] you're not good at processing this, and there's a certain level of continuous activity you need to do to get those adaptations. That somewhat confuses the interpretation of the data.

Whereas blood lactate is more of a metabolic level, it's your biological level. Because when your lactate levels increase, it means you're reverting to anaerobic fermentation or glycolysis in the cytosol to generate lactate. And that usually is correlated with reductive stress, because lactate is a reductant. And when you have reductive stress, your electron transport chain does not work that well. It gets really slowed down. So, that makes perfect sense, the lactate levels. And you can actually measure the lactate-to-pyruvate ratio, the NADH-to-NAD ratio, and reduced-to-oxidized glutathione ratio, probably CoQ10, the same thing. So those are different ways that you can assess what's going on biologically, but it would seem that the lactate levels, they're not related to this training effect that you'd have to do if you're exercising to get that. So I don't dispute that the VO2 max is a useful tool, but I think it needs to be interpreted in the context of all those other variables.

**Dr. Arkadi Prokopov:**

Yes, but there are some details. First of all, a physiological level of lactate is pretty, pretty high in healthy people with healthy mitochondria. Because lactate, especially for instance, in the night, it's [a] very important fuel for [the] brain, for neurons, for astrocytes and also for our heart. So, lactate is not only an energy-giving fuel, it has also [a] signaling function. It has many functions, not only as a fuel.

**Dr. Joseph Mercola:**

Yeah, but is it-

**Dr. Arkadi Prokopov:**

On the other hand, when you're running, of course, first you run – the most economical run is when you're burning fat. Absolutely. All marathon winners, they run on fat, and they save glucose for the last acceleration.

**Dr. Joseph Mercola:**

Yeah, the sprint, the last bend.

**Dr. Arkadi Prokopov:**

For the sprint. And then they have increased lactate levels because they go over [the] anaerobic threshold. So, I think these are different mechanisms and I don't see any contradictions here.

**Dr. Joseph Mercola:**

Okay. All right. So, I'm assuming, though, that there should be the same modulation, this peaking and trough of the lactate levels as it is with the fuels. And so, what – let's finish up on the fuels first. What is the, in your extensive experience, what is the optimal time for intermittent fasting? What is the window that – and I know it takes a while. The average person can't do that, 95% of the population is metabolically inflexible, and they have to adjust to this. A few 5% can do it, but you know, most people can't. But if you were healthy enough, what would be the optimum? Is it like you shouldn't eat – I mean, [Dr.] Satchidananda Panda out of Salk Institute has done a lot of work in this, and he says that you should not eat more than 12 hours a day. When you do, that's going to be a problem. And you should go up to maybe 16, maybe 18 hours a day that you don't eat. So, what is your experience and recommendations in that field?

**Dr. Arkadi Prokopov:**

An average recommendation is 8/16.

**Dr. Joseph Mercola:**

Okay, 16/8.

**Dr. Arkadi Prokopov:**

Yeah, 16/8. So, 16 hours without food, and during eight hours, you can eat. Of course, with more experience, with improvement of metabolic flexibility, which is 100% dependent on mitochondria, you can narrow it instead to six hours, just one hour a month can be compressed. And I personally have maybe five to four hours meal window. And it's very good, synergistically works with hypoxic training.

**Dr. Joseph Mercola:**

Oh yeah. So, I used to do that too, until I encountered Ray Peat's work. And that butts up against this whole concept that when you don't have glucose to fuel the mitochondria – and maybe you can help me understand this, because it may be a non-issue if you have a healthy liver, because your liver is the primary source of the glycogen, which is the polymers of glucose that would supply your body with sugar when you're not eating. And if you have a healthy liver, you probably can go more than a day and still have healthy glucose levels.

But once you deplete your glycogen levels, then you have to activate your stress hormones and you have to activate glucagon, adrenaline and cortisol. And those stress hormones are pathologic, and if done continuously at high levels, then it will accelerate premature death. There's no question in my mind. They're bad news. Specifically cortisol, it just sucks out the amino acids, the protein from your tissues, decreases bone density, decreases muscle mass. It's bad news. So, have you heard that argument? And if you have, how do you reconcile that?

**Dr. Arkadi Prokopov:**

Yeah, this is a very, very important issue. First of all, gluconeogenesis is an extremely important evolutionary biological mechanism because, you see, if we take, let's say, an herbivore, some cow or deer, and we measure the glucose level, it's about 100. About [same] as we have in our

blood. But if we take a cat or a lion, and if we measure glucose level, it will also be about 100. Why? They don't eat any carbohydrates? So they get glucose from gluconeogenesis, and gluconeogenesis consumes amino acids.

**Dr. Joseph Mercola:**

Yeah, that's the cortisol. It's what it does.

**Dr. Arkadi Prokopov:**

No, for gluconeogenesis?

**Dr. Joseph Mercola:**

Yeah, that's how you turn it on. I understand this.

**Dr. Arkadi Prokopov:**

The amino acids – in the liver, there is a process of germination and there is synthesis of glucose. Normal liver produces about 180 grams of glucose a day [inaudible 00:44:14]-

**Dr. Joseph Mercola:**

Or more.

**Dr. Arkadi Prokopov:**

Even more.

**Dr. Joseph Mercola:**

Yeah, most people don't know that. Yeah.

**Dr. Arkadi Prokopov:**

But you should be healthy enough. You should be metabolically flexible. You should have good mitochondria, then it functions perfectly.

**Dr. Joseph Mercola:**

But here's the point, in order to flip that switch and produce those, you have to activate it. And you activate it by releasing the stress hormones — glucagon, adrenaline and cortisol. And those stress hormones have negative adverse consequences on your biology if activated chronically. There's no question you can get really healthy glucose levels by doing it, but you're going to do it at a price. So, your body wants to fuel continuously and it will set – If your blood sugar drops too low, you are dead. Yes, lactate can fuel your brain. Yes, ketones can fuel your brain. But it needs glucose. Without glucose, you're dead. 100% you're dead.

**Dr. Arkadi Prokopov:**

I do agree. I do agree because our erythrocytes, red blood cells, they have no mitochondria. They survive exclusively from glucose. Yeah, that's true. But stress hormones, when they are continuously released, of course it's a catastrophe.

**Dr. Joseph Mercola:**

That's what I'm saying.

**Dr. Arkadi Prokopov:**

Whereas a pulsatile release, stress and then relaxation, for repair, for recovery. Stress and then relaxation. This is like periodicity in training of endurance athletes. If they're overstressed, they got injuries, they got chronic injuries, then their aerobic power will be reduced. But if the properly organized training, they have recovery periods when they replenish all the exhausted hormones. And of course, it's the combination of stress and relaxation, stress and relaxation. Any continuous stress depletes hormones, exhausts steroid hormones and reduces oxidative stress.

**Dr. Joseph Mercola:**

Alright, so I think I figured it out. In my attempt to explain the dilemma, or at least my perceptive dilemma, I answered the question. And it's related to your liver's ability to store glycogen. If you have sufficient glycogen stores, you can go for 16 hours without eating and not activate your stress response. If you go for a lot longer, specifically, certainly after two days or three days – 100% almost everyone over three days, no one has that much glycogen stores – then the only way to stay alive is to activate the stress hormones. But here's the caution, the caveat, I think, and I'd like your input on it, is that a third, 40% of the people have liver disease, they have NAFLD, nonalcoholic fatty liver disease. And that impairs your body's ability to actually produce glucose through gluconeogenesis and store it as polymers in your liver. You just can't store as much. So, then you have to be more careful. You have to be really careful because – fortunately, and usually it's things like linoleic acid, omega-6 fats, and too much estrogen, those damage the liver big time. And toxins, of course. But if you have a damaged liver, it's not going to work as well.

**Dr. Arkadi Prokopov:**

Yes, of course. Yeah.

**Dr. Joseph Mercola:**

Yeah. Well, maybe not "of course," not "of course." To a lot of people, they don't get that. That's a big issue because liver disease is pervasive.

**Dr. Arkadi Prokopov:**

Yeah. And I think that this pandemic of liver disease now, it's a continuation of metabolic inflexibility.

**Dr. Joseph Mercola:**

Yes, yes. A hundred percent, [inaudible 00:48:01]-

**Dr. Arkadi Prokopov:**

In the nature, there are always periods of lavishness and fasting. There is nothing to eat for days, sometimes weeks, and animals survive, and people also survive. [A] sign for very long fasting. You know, there is a very successful cancer survivor who survived just because of prolonged fasting.

**Dr. Joseph Mercola:**

Yeah. I'm not disputing that those exist. I don't think that's the optimal strategy, though. I think that you run into the risk when – because when you do that strategy, you are activating stress hormones 100%. There's no way you can go more than two days and not activate your stress hormone. It's just biologically impossible. So, you have to counter the benefit, and there is a benefit against the downside, and it's a balance. You do too much and it's going to be problematic.

**Dr. Arkadi Prokopov:**

It's always a tradeoff, of course. You need just to balance it very finely.

**Dr. Joseph Mercola:**

Yeah.

**Dr. Arkadi Prokopov:**

You need to monitor symptoms, clinical symptoms, listen to your body. That's the success of treatment of very serious chronic diseases.

**Dr. Joseph Mercola:**

Yeah. All right. So, I think you've helped me understand just the dialogue with someone who's really, really smart about mitochondrial function. The people like you are few and far between. Your level of expertise is pretty extraordinary. So, I appreciate the opportunity to speak with someone like you. You helped me understand it.

**Dr. Arkadi Prokopov:**

Thank you. Thank you very much. Actually. I'm [a] biogerontologist also. [The] first application of intermittent hypoxia is antiaging intervention. I made [a] presentation in 2008 in Cambridge, by Aubrey de Grey, [from] SENS Foundation. But since then, I have seen that it works much more obviously in problematic conditions, which are really, really dominating now. For instance, Lyme disease, borreliosis. I've applied this treatment since 2006. I now have more than 200 patients with chronic Lyme cured basically with intermittent hypoxic training, of course, also nutritional components and some necessary [inaudible 00:50:32].

**Dr. Joseph Mercola:**

Yeah, I don't doubt it. And you can probably add dozens and dozens and dozens of other diseases. No question-

**Dr. Arkadi Prokopov:**

Yeah, because it's all about [the] mitochondria.

**Dr. Joseph Mercola:**

It's all about [the] mitochondria, 100%. But I want to explore something with you now, because we've got limited time left. I want to propose to you an idea that if you could run – I can't do this because first of all, I'm not a scientist, and I'm discredited in the scientific community. I'm just blackballed. I couldn't do a darn thing with this. But you could. I believe there's several Nobel Prizes in this. And I really appreciate your passion about longevity and biogerontology, as you've mentioned. There's no question intermittent hypoxia training works. It's my speculation that it's working largely as a result of increasing CO2 levels.

And there are other benefits, I'm not saying it's the only one. No question there are other benefits. But the increased CO2 level is where the magic is. The CO2 does it in a few different ways. Primarily because it forms this cloud – the CO2 directly attaches to the proteins, specifically lysine and histidine, and it forms this electric cloud over the protein that protects it and it actually modulates the functional expression of that protein, which are typically hormones. Most of the hormones are proteins. So, you can activate them [inaudible 00:52:00]. You just radically increase the efficiency of the proteins and hormones in your body.

And then that's why I asked the question about the histones. The histones are proteins, too. And these are the proteins that surround the DNA, nuclear DNA, and they modulate the expression. So, it's epigenetic control of your body's ability to produce proteins in your body. Have you heard of Akkermansia before? It's been around for 20 years.

**Dr. Arkadi Prokopov:**

Yes, of course. Akkermansia, I gave it to my patients.

**Dr. Joseph Mercola:**

Okay, good. So you knew about it. So, an Akkermansia works primarily because it increases insulin-like substance, specifically GLP-1, glucagon-like peptide, and it helps modulate control. It's actually been approved now. It has FDA indication for treating diabetes and, by secondary implication, obesity. So, if you can – and population is normally supposed to be about 10% of your microbiome, but most populations now have like less than 1%. So, the key is not to take a magical Akkermansia probiotic – and they exist and they do help. But the more effective strategy is to give them the fuel, which will be fibers too, if you don't have a problem – because one of the one of the things when you have microbial imbalance in your intestine, you have an excess of gram-negatives, and the gram-negatives are the ones that produce endotoxin, LPS, lipopolysaccharide.

And when you have too much of that, that will destroy mitochondrial function. That and omega-6 are the two primary culprits that destroy mitochondrial function. No question. So, the key is to modulate that endotoxin production. And interestingly, Akkermansia is a gram-negative bacteria that does not make endotoxin. It doesn't make it. And when you augment the production of

Akkermansia or Akkermansia-like [inaudible 00:54:57], because there's probably more, that's just the biggest one. But when you increase the production of these, there's a microbiological principle. It's called competitive inhibition.

So, they grow and they crowd out the other bad guys. So, you radically reduce endotoxin when you do that. So, [there's] a number of different mechanisms. I just think that the CO2 – I mean, it's not in place of, it could be done in conjunction with something like intermittent hypoxia training. And I think the mechanism would enhance it, and it's just the other hidden value of CO2. But I think it all relates to the CO2. It's my belief that CO2 intervention is the single best longevity hack I've ever encountered. It's CO2. So, what is your – I gave you a long dialogue. I was really appreciating an expert like you [who] knows the field, this is your discipline. What do you think about that?

**Dr. Arkadi Prokopov:**

I think that, of course, it's very interesting, extremely interesting. But why not use CO2? Because we have CO2 puffs-

**Dr. Joseph Mercola:**

A hundred percent. Yeah.

**Dr. Arkadi Prokopov:**

We have CO2 injections in the skin, hypodermic injections. So, it's an old, very well-known option. In [the] U.S.A., by the way, there were also some scientists and practitioners who used it. I know, for instance, there was Laszlo Meduna, who wrote a very thick book about his experience with carbon dioxide inhalations.

**Dr. Joseph Mercola:**

Yes. That's different. Not as good as-

**Dr. Arkadi Prokopov:**

Yeah. It's very extreme. There are many facets of CO2. For instance, it works as a very important guard of our genome, at all.

**Dr. Joseph Mercola:**

For sure.

**Dr. Arkadi Prokopov:**

The most extensive damage for a genome is from peroxynitrite.

**Dr. Joseph Mercola:**

Oh, yeah.

**Dr. Arkadi Prokopov:**

And CO2 neutralizes peroxynitrite.

**Dr. Joseph Mercola:**

I did not know that. Do you have any papers on that?

**Dr. Arkadi Prokopov:**

Oh, yes. There's a lot of publications. Especially because continuous –

**Dr. Joseph Mercola:**

Geez, I did not know that.

**Dr. Arkadi Prokopov:**

The problem is if there are impulses from free radicals and nitrous oxide and all, that's very important. This is killing viruses, bacteria, and it also participates in signaling. But if the both are continuously stable on the higher level, it damages all around, because peroxynitrite damages [the] genome.

**Dr. Joseph Mercola:**

Well, it damages everything. It's massive-

**Dr. Arkadi Prokopov:**

So, CO2. Of course, CO2 is helping to neutralize, so it just supports genome stability and it automatically means it slows down [the] aging process.

**Dr. Joseph Mercola:**

Yeah. It also supports the histone. It modifies the proteins in the histones, the [inaudible 00:58:57] amino acids.

**Dr. Arkadi Prokopov:**

Yeah.

**Dr. Joseph Mercola:**

And there are two mechanisms. And for those who don't know, it's the nitric oxide that combines almost instantaneously – I mean, it's almost unmeasurable – with superoxide to form peroxynitrite. And the half-life of that is – I think it's a million times longer than the hydroxyl radical. It's not as potent a reactive oxygen species, but collectively it is because it lasts so much longer. It could actually travel outside the cell into other cells, which is just extraordinary. Normally, hydroxyl radical only travels like the distance of a protein and it's gone. It just doesn't last. So, it is a localized damage typically in the mitochondria. But this peroxynitrite is bad news. It's bad news. If I just look it up on PubMed, would I find that association [with] peroxynitrite?

**Dr. Arkadi Prokopov:**

I can send you links [and] publications. Yeah, I have them.

**Dr. Joseph Mercola:**

Yeah, that's pretty good. Ray Peat was one of the biologists who brought this knowledge to the forefront, and he used some examples of mammals, like the naked mole rat, who's a common example in longevity research and also bats that live 10, 20, 30 times longer than their other equivalent in – Yeah, so what's the mechanism? There's a good suggestion that it might be CO2.

**Dr. Arkadi Prokopov:**

CO2 in naked mole rats, absolutely clear. They have hypoxic hypercapnia in their dwellings.

**Dr. Joseph Mercola:**

Yes, absolutely. Yeah.

**Dr. Arkadi Prokopov:**

Yes, it's clear. It was measured, it was shown. But there are, of course, some evolutionary mechanisms, which are outside of this. Because bats, they live in ventilated caves. There is no hypercapnia there.

**Dr. Joseph Mercola:**

Yeah, yeah.

**Dr. Arkadi Prokopov:**

But they undergo hypothermia. They're extremely well – they are metabolically flexible till extreme, because they can induce hypometabolic state, and of course, this state slows down [the] aging process.

**Dr. Joseph Mercola:**

Okay. Well, good. This is good. All right. So, if someone wanted to explore intermittent hypoxia training, what are your recommendations? And how could they find more about what you're doing?

**Dr. Arkadi Prokopov:**

Well, they can just go to my website.

**Dr. Joseph Mercola:**

Okay.

**Dr. Arkadi Prokopov:**

Go to my website. Just type in Google "Arkadi Prokopov," and they will find I have a lot of videos with explanations, and now I'm preparing educational seminars for physicians in English. So, it's under development.

**Dr. Joseph Mercola:**

Oh, good. Well, I want to thank you for all your kind work and this has been great. I was so looking forward to talking with you.

**Dr. Arkadi Prokopov:**

Thank you. Thank you for [the] invitation. It was [a] great talk.

**Dr. Joseph Mercola:**

Yeah, yeah. Good.