Introduction to the Cell Danger Response

Welcome back to the conquering Chronic Inflammation Summit. I'm your host, Doctor David Jokers. And today I've got the honor of interviewing Ari Witten.

And we're talking about the cell danger response, mitochondrial function and healing with hermetic stressors. This is a deep dive into how our cells operate, particularly when they're under chronic stress, and how and the link between mitochondria and chronic inflammation.

And we're gonna obviously go through what we need to do to heal naturally. Ari Witten, if you don't know him, he's a founder of the Energy Blueprint. He's a bestselling author of The Ultimate Guide to Red light Therapy and Eat for Energy How to Beat Fatigue and Supercharger Mitochondria for All Day Energy.

He's a tireless researcher who has obsessively devoted the last 27 years of his life to the pursuit of being on the cutting edge of the science on health and human energy optimization.

And you can find his podcast programs and supplement formulas at the Energy blueprint.com. So without further ado, let's go into the interview with Ari Witten.

Well, are you kidding? Always great to connect with you and, always enjoy our conversations. And one of the main topics I love talking with you about is the cell danger response.

Because really, not many functional practitioners or conventional, I mean really conventional doctors. This isn't even on their radar, and most functional practitioners aren't even really aware of it, or at least not able to communicate it effectively.

But this is a it's really the way that we need to start looking at complex chronic illness, chronic inflammation. And it's essential to really understanding physiological processes in our body.

And so let's break this down. Cell danger response and its relationship with chronic inflammation. Okay. So that's a big question. Let's see where to begin.

The cell danger response is it's a model. A hypothesis. And a way of conceptualizing what's going on physiologically in health and disease states. And it comes from, researcher and MD, PhD, who runs a lab for mitochondrial medicine at the University of California, San Diego, named Doctor Robert Navajo.

And I think about ten years ago, he published sort of the seminal paper that was called The Cell Danger Response. And this was the first outline of this model, this way of understanding, disease and health processes and, and he, he puts this really at the center of the vast majority of disease processes.

Mitochondria as Energy and Defense Hubs

He's since published a number of papers since then, developing this model, adding new layers of insights to it, also testing it, you know, testing lots of of things related to it in his lab in, at UCSD.

And I think the most recent paper, came out in 2023, which was titled, let me see if I can find it, mitochondrial and metabolic Features of salad Genesis and the Healing cycle.

I particularly like this because cell eugenicist or Soludo Genesis, which is the genesis, the creation of health as distinct from pathogenesis, the creation of disease processes, which is the focus of really the entire entirety of, of modern medicine, is a big focus of mine at this moment.

So, the basic idea of the cell danger response has a lot to do with mitochondria. Okay. Mitochondria are, in Doctor Navios words, the central hub of the wheel of metabolism.

The metabolism is a word that most of us kind of associate with, like weight loss. And you know how many calories we burn. But the actual meaning of that word that's resting metabolic rate, right.

And that word has been has sort of morphed into metabolism. But the true meaning of the word metabolism is actually all of the biochemical reactions that occur in your body, like basically everything that's going on in your body, everywhere in your body is metabolism.

And, what what Doctor Navias is saying is that mitochondria are the central hub of all of this, of everything that's going on in your body, which is this in itself is a really important thing to understand, because the way we all learned, like you and me and all of our friends and colleagues, we all learned about mitochondria starting, you know, in grade school and in high school and in college and in graduate school, in physiology and in medical school.

All all of these things, it was taught to us as really just the powerhouse of the cell. That's the thing we got to remember on our exams. We learned the electron transport chain.

We learned how mitochondria turn, fuel carbohydrates and fats, ketones into energy in the form of ATP. But really, they're framed as these sort of mindless cellular energy generators that really all they do is they take in fuel from our food and they pump out ATP.

And that's kind of you learn the different process of NAD and fad H and, you know, this whole electron transport chain stuff and CoQ10 and blah blah blah and ATP synthase and it pumps out ATP.

But really the whole thing at the end of the day is, is really they take in fuel, they pump out energy. They're mindless cellular energy generators. And what Doctor Navios work did with the cell danger response was synthesize a huge body of evidence that has been accumulating over the last 2 or 3 decades, from researchers all over the world on the other roles of mitochondria, like all these other things that might occur that we've been discovering that mitochondria do.

And it turns out they do a lot of different things in our body, and they're really important to almost everything that you could imagine. And you can you can learn this really quickly by sort of googling, any medical concept you can think up or any disease you can think up and mitochondria and you'll probably find a whole bunch of papers on that now.

So the, the, the, the simplified idea of the cell danger response is really that, and I'm removing a lot of the complexity here intentionally for the sake of understanding.

But the basic idea is that mitochondria actually have two major roles. One is the story that we were all told in our education, which is energy generators.

Okay? They are these things that they do take in fuel. They pump out energy. Okay. That's one major role that mitochondria have. The other major role that they have is in cellular defense.

And it turns out that they are basically functioning as the canaries in the coal mine of our body. They are these sort of exquisitely sensitive environmental sensors that are constantly taking samples of what's going on inside the cell, in the environment to perceive the environment.

And they're asking the question, is it safe for us to produce energy? Okay, they're trying to get a picture of whether the body is under threat or under attack in some way.

And if it isn't, then they're going to operate in what Doctor Navajo calls peacetime metabolism, and they're going to produce energy in abundance. And everything's great.

However, to the extent that they pick up on danger signals, on threat signals that the body is under attack in some way, and we can talk in detail of what what that means and how it how it's sensed.

To the extent that they pick up on the signals and to the extent that those signals are perceived to be an overwhelming threat that surpasses their capacity to deal with that threat, then they shift from energy mode, from peace time metabolism into war time metabolism, into the cell danger response.

And what that cell danger response is all about is fighting off and combating the threat and protecting the body as much as possible from that threat.

And what what happens in this state? The first phase of the cell danger response, which is really the most important phase, this is this is sort of the crux of what the cell danger response is, is it really revolves around, okay, we're battening down the hatches.

We are trying to decrease the amount of signaling and communication going on. We're shutting down cellular energy production. We're throwing off lots of oxidative stress.

What Keeps the Body Stuck in Chronic Inflammation

We're creating lots of inflammation to signal for our immune system cells to to come in to this area, which might be the whole body or might be systemic in the blood, or might be localized to a particular area.

We're signaling for the immune system via oxidative stress, via inflammation, to attack, to defend the body and combat this threat. Okay. So, as an analogy, imagine that, you know, you're in your house and, you're preparing dinner, you're chopping vegetables and you're making dinner for your kids, and then, criminal breaks and puts, puts a gun to your head, says, give me all your money, give me all your valuable stuff.

You're not just going to keep chopping vegetables and preparing dinner as normal. You have to to stop doing that. You've got to deal with the threat. So to to the extent that the body is under attack and under threat, it's turning down the dial on all of the normal healthy metabolic processes and energy production in particular, and switching to a mode of defense, wartime metabolism and combating that threat.

So it's important to understand these two modes energy production mode and defense mode. The cell danger response are mutually exclusive to the extent you're doing one, you're not doing the other.

Yeah, it's a great explanation. I think, about the mitochondria as the nervous system of the cell, basically like the brain and nervous system. And so we used to think they just had a motor function, kind of like your nervous system tells your arm, you know, your bicep to flex.

But we know the nervous system was constantly taking in input. Right? And adapting to the environment around it. And that's basically what the mitochondria are doing.

They have an affair and efferent or a, a a sensory and motor function. And they're adapting to basically give us the greatest possible survival advantage.

And in some cases that means turning up oxidative stress in fact happens often turning up oxidative stress, which is a precursor to inflammation and turning up inflammation. But that should be for a short period of time until we complete the healing cycle and return back to a peacetime physiology.

But there are many factors that can keep us in this wartime physiology. And when we're stuck in that, when we when we have an incomplete healing cycle, we're stuck in this wartime physiology, that's when we end up with, over time, chronic inflammatory conditions.

And so what are the things where some of the main factors that, hey, that was that was a great stuff. That was a great follow up to everything I explained.

That was like the the next layer of what I was going to explain. We're like, tag teaming this. That's why I've been studying this for a while now too.

And, you know, credit to you as well. You're one of the people that turned me on to the saw danger response. And as you know, once you go down this rabbit hole, you know, it's really fascinating.

And it changes the way you view how the body adapts. And so it's something I've been studying and really doing my best to try to be able to communicate as well.

Awesome. You're doing a great job. Great. So let's go into things that can keep us stuck in that cell. Danger response and incomplete. Basically, you know, we need to complete the healing cycle.

If we don't what obviously that that's going to lead to chronic inflammation. So what keeps us stuck in the cell. Danger response okay. So, you know, there's there's a simple and short answer to this, and there's a longer, more complex answer.

And there's a whole lot of nuance and potential complexities that could be involved as well. The very simple and short version is if the stressors that are inducing the state of cell danger response in the first place are continually present without letting up, then you can expect the cell danger response to be more persistent or chronic, or the body to get stuck in that place.

So as an example, you know, we can think of the cell danger response, the normal inflammatory process in the context of, let's say acute, an acute injury, like you're playing soccer, you sprain your ankle, you've got inflammation and swelling and redness, and you've got an inflammatory response in that area.

Immune cells are activated to to take care of that, and repair the damage. Or the same is true like in the context of common cold or flu or Covid or, you know, in the context of an infection, you got this transient activation for several days, maybe a couple of weeks, to deal with the threat.

And then you have resolution and this is the cell danger response phase two and phase three. And then ultimately getting back to health and normal function.

So this this is a cyclical process health okay. Now we've got to deal with a threat cell danger response one cell danger response phase two three. And back to health okay.

And that's that's designed that that's how this system is designed to function and functions very well in the context of acute stressors, injuries, infections, most things that where we are designed ancestral lead to deal with now this picture.

So in the modern world this picture changes. And we sometimes have different stressors that we can be exposed to that are relatively chronic or persistent.

So for example, if we've got, heavy, you know, heavy metals, exposure that stays stuck in our body for a long period of time. If we are chronically getting exposed to mycotoxins from the place we live, or if we're getting exposed to other toxins from our food, from our water supply, from the air we're breathing constantly.

And we are not escaping that, you know, if it's sort of just a chronic, never ending, unrelenting onslaught of stress that the body is trying to deal with, we can't expect it to return to health and normal function because it's still trying to deal with those threats.

So it hasn't had the time and the space to be removed from the sources of stress to be able to recover. So that's the very simple version of it is as long as you have these stressors that have triggered you into the cell danger response in the first place, still present in your life, you can expect to stay in the cell. Danger response.

The more complex answer to this is we have to. I'll explain two models of ways of understanding conceptualizing

disease. So one is called the Allostatic model.

Allostatic load model of health and disease. And this this is the dominant model, the way that most people in functional medicine and natural health tend to understand health and based.

The basic idea is the more we have total body stress load from toxins, from sleep deprivation and circadian rhythm disruption, from psychological stress, from all sources, from relationships, from our job, from, you know, traffic jams, from whatever we're dealing with.

The more we have a poor diet, the more we drink alcohol, the more we smoke, the more we, sort of get all the the fundamentals wrong in the way that we are living and the environment we're in.

The more we have these stressors that are, impinging on our body's ability to maintain homeostasis. And this is basically called allostatic load or total body stress load.

And at a at a certain point, at a certain threshold, when those when that allostatic load gets big enough, the body stops being able to maintain homeostasis.

Allostatic Load and Physiological Resilience

Okay. And then and then we have the beginnings of symptoms and disease and our physical decline. Okay. And that's that's a really good, useful, and highly accurate model and way to understand human health.

But it doesn't go quite far enough. And there's a better model that is not very well known. Outside of geoscience circles, geoscience is the study of human aging, the study of aging in general.

And this is called the Homo dynamic space model of human health. And basically the whole geodynamics space model incorporates everything from the allostatic load model.

For the most part. But it adds one layer to this to to the discussion, which is what is the organism's stress buffering capacity. So resilience. Yes, exactly.

So the allostatic load model generally says okay, we've we've got, you know, these stressors, these stressors cause disease. What do we do to fix the situation?

We do our best to remove these sources of stressors on the organism. Great. Awesome. However, what's missing from this picture is resilience through resilience and the the the ability to resist these stressors without being damaged by them is also central in this picture.

And the more that you understand what resilience actually is physiologically and how the modern world affects it, the more you realize that physiological resilience is actually just as big of a player in this discussion as all of these different stressors of the modern world.

So what we really have, and I'll tie this back in to the cell danger response. What we really have is, yes, we've got a modern world, an environment that have a high allostatic load, that strain the body's ability to maintain a state of health and homeostasis.

And we've also got a modern world and a modern lifestyle that drives loss of physiological resilience in numerous of the systems of our body that are critical in resisting the negative effects of these stressors, the allostatic load and what that does is it shifts the balance to make us much more easily overwhelmed by these stressors in in our life and in our environment.

And when if you remember what I said earlier when I was describing the cell danger response, it's when the mitochondria perceive themselves to be under an attack, under attack to a degree that they don't have the capacity to deal with.

And that was an allusion to physiological resilience. So that picture, more allostatic load, less resilience leads to a situation where we are much more likely to be overwhelmed by the stressors in our environment and to be stuck in the cell. Danger response.

So there's two things we have to fix. We have to minimize and reduce and eliminate the sources of allostatic load as much as possible from our from our life.

And we have to build resilience back into our physiology in order to shift ourselves out of this chronic state of inflammation, this chronic state of the cell danger response.

That's a great explanation. You said that that theory is the homo dynamic. What was it, the homo dynamic homo dynamic space model, space model. And so if we were to put that into a math equation, from what I'm understanding, you saying, if we if it was like a division problem, the, the overall allostatic load or kind of the cumulative effect of toxins, infection stressors on our body would be at the top.

I can't remember what the numerator denominator is. So it's at the top. Yeah. And then it's being divided by your overall stress resilience, which would be pretty much determined by the amount of healthy high functioning mitochondria within the cells of the body.

I would imagine that would be, a big factor when it comes to your overall stress resilience. And that would be at the bottom. Right. So the so it would be being divided by that and the higher overall number, you know, so equal to the higher overall number would be more of in a sense the downward pressure causing causing causing you to stay stuck in the cell.

Danger response developing chronic disease. Whereas the lower the number because you have a higher number at the bottom, the division number lower allostatic load at the top, the more overall resilient your body is and the lower the potential for developing chronic illness, I believe so, and and I say that because I've never conceptualized this, in terms of math.

Well, that's why we're having conversations like this, you know. So I'll tell you, I and I certainly understand what you're what you're getting at here.

And I'll tell you how I think about it. So, and I'll give some examples. I think I'm going to put that into an infographic and send it over to you. Yeah. There are infographics on this.

If somebody wants to do a Google image search. So what the infographics that I like generally show are let's imagine that we have a line here that is our threshold for where we stand.

So like a picture or a bar graph okay. So we have a line here like through the middle of the graph. That is our threshold where if if we go below that line, in terms of our resilience, we now have basically let's see how I want to explain this.

This is sort of the critical threshold. And if you go under this capacity, this threshold, you start to get the beginnings of disease processes. Okay.

So this this this bar represents your stress buffering capacity and if it shrinks to the point where it goes below this bar, now you've got the beginnings of disease.

Okay. So mitochondria play a central role in this. I'll talk about that in a minute. But I'll give another example, because actually this principle extends to almost every system of the body.

And this is actually the subject of the book I've been writing for the last year. But you'd be shocked at how many different systems of the body this applies to.

So I'll give one example here. There's something in that that is in the literature called cognitive reserve capacity. It's

also called is another distinct concept in the literature called brain reserve capacity.

These two things are actually much more overlapping than a lot of the literature. Sort of indicates or tries to imply. But basically what this is, is the concept that I'm describing.

It's the homo dynamic space of the brain. Now what builds this homo dynamic space of the brain, this cognitive reserve capacity turns out learning the things builds your cognitive reserve capacity.

Learning things, learning new things, challenging things, challenges the neural circuitry of your brain, much like lifting heavy weights, challenges your muscles to grow bigger and stronger.

And in response, they do grow bigger and stronger. The neural, the neuronal circuitry of your brain literally, structurally grows stronger. And this is mediated by a whole number of things different, different molecules, dendritic spines, better connections between neurons, specific neurons and networks of neurons, and the actual physical structural robustness of certain areas of the brain.

Mitochondrial Reserve Capacity and Aging

And that that's, you know, you can actually see if you do a brain scan and this cognitive reserve capacity, came to be discovered basically because they found that people who had more education in their life, more formal education, were were strongly protected from neurodegenerative diseases like Alzheimer's and dementia.

Okay. So learning things like going to school and learning things, or learning a language or learning a musical instrument or even learning physical things like dancing or a sport, it creates more cognitive reserve capacity in the brain, which actually translates into being able to resist a lot of the forces that would otherwise degenerate the brain and end up with, with, giving you dementia or Alzheimer's dementia.

Okay, so if you picture that, that bar graph that I described before, and here's the cutoff for where you start getting Alzheimer's or dementia and somebody with high cognitive reserve capacity who has spent a lot of their life engaged in active learning and education, is way up here in terms of their stress buffering capacity.

So they can go many, many more years and endure a lot more stress on that system before they ever get down to that, that threshold where they're going to start exhibiting dementia and Alzheimer's disease, where somebody with much lower reserve capacity in their brain is has a much smaller window of time and much smaller capacity, to endure stress on that system before that system degenerates to the point where now you're exhibiting Alzheimer's disease and dementia.

So this this is a spectrum, and it is about your physiological resilience and capacity to endure stress on that system, whether it's biochemical stress, whether it's toxins, whether it's sleep deprivation, any any type of stress on that system, your capacity to resist it without being damaged and to resist it long enough that it ends up not being the thing that kills you.

Now, that principle that I just described, again, I'm writing a book basically. You know, one chapter of the book is on cognitive reserve capacity, but the other chapters are on all the other physiological capacities.

And the different areas of our body, and how they protect us against disease and bolster our health and longevity. But mitochondria, as you said, are also central to this story.

And, this is, a bio, our bio energetic reserve capacity. And one of the things that we have to understand is, basically any type of stressor you can imagine, any type of stress on that system is creating a bio energetic stress on that system.

So whether it's toxins, whether it's sleep deprivation, whether it's even healthy things like exercise or learning things like I just described in the brain, and all the sources of bad stress and allostatic load, you can imagine they are all creating an energetic stress on on the cells of the body as well.

And the capacity of your mitochondria to meet that and, and handle that energetic stress or not handle it is a huge determinant of whether you will end up with your mitochondria shifted into the cell danger response.

So let me let me give you another data point to overlay on this. It's been shown in a number of studies that the average 70 year old has lost 75% of their mitochondrial capacity.

Okay. And this is a combination of, of of two things. The mitochondria themselves are shrinking, physically shrinking to about half the size and the number of mitochondria that are present.

Purcell are also being reduced to about half to half the size. And the combination of those two things, if you do the math, since your math guy apparently, better than me, the combination of those two things is a loss of 75% of your mitochondrial capacity.

Now, I hate percentages because it doesn't really do this justice to for people to really get this. What this means is that if you were at 100% capacity when you were 20, and you're now at 25% of your capacity, this is like going from a Ferrari V8 engine in your cells when you were 20, to a moped engine in your cells when you're 25.

Do you think that that affects your ability to resist and to handle or resist bioenergetics stresses to to to resist the forces of stress on that system?

Absolutely. Absolutely. It affects it to a massive, massive degree. And this is fundamentally why, mitochondrial dysfunction, this kind of buzzword, in, in, in natural health now is linked with so many different disease processes.

Yeah, yeah. For sure. I always say the quality of your life is going to come down to the amount of mitochondria and the quality of the mitochondria, because there's a big difference between a senescent mitochondria, which all of us have to some degree, and a young, very stress resilient mitochondria.

There's a night and day difference there. And so you may have a certain amount of mitochondria, but the high percentage of those are senescent or age dysfunction or mitochondria in a sense, your overall functionality and your stress resilience can be a lot lower than somebody that has the same amount of mitochondria.

But a higher percentage of stress resilient, high functioning mitochondria. That's right. Yeah. And and I'm glad you brought that up because. I left one key point out of the story that I just told, which is, as you just imply, the the quality and quantity of the mitochondria in our cells is highly malleable.

And this, this picture I just painted of losing 75% of your mitochondrial capacity as you get older, is actually just the average of what normally and typically happens, to most people.

Okay. And what this isn't is a claim that quote unquote aging does this to our mitochondria in a sort of biologically predetermined way. Actually, it's the opposite.

And here's here's the good news, because you're probably feeling really, like this is really bad news, learning that your mitochondria, mitochondria and mitochondria capacity decline so much with aging.

If that's got you feeling down, here's the good news. The good news is, when we look at 70 year olds who are lifelong exercisers, they have the same mitochondrial capacity as young people do.

So, this is not a functioning a function of aging per se. This is a function of our lifestyle. And what's really going on here, in terms of mitochondrial size, mitochondrial quantity and quantity is that, this is fundamentally a product of the way we live and specifically the degree of demand we put on those systems.

So in the same way I could I could tell you, and this is much easier for people to understand because it's much more outwardly visible. As soon as things start going down to a smaller level.

Humans kind of make the mistake of thinking, oh, you know, this is driven by mysterious biochemicals, and I need

to take a drug for this. But when it's big and outwardly visible, we have a much more time with the logic of understanding things in the proper way.

Muscles. Okay. So, with muscles, if we challenge our muscles by lifting heavy objects, what do they do? They interpret this as a stimulus to adapt to this challenge by growing bigger and stronger.

It's a survival stimulus. So, in basically, they're going in order to better handle the challenges of my environment, to better survive my environment and to be less damaged by the stress of my environment.

I need to to adapt to these demands by growing bigger and stronger muscles. Okay. That the the opposite is also true. So and this is the down. So I before I get there, this is actually an amazing thing if you understand.

Like if you look at a chair or a bicycle or a car or any sort of other object in our environment, any inanimate object, they don't do this, okay? They don't have the capacity to sense and adapt to the demands on them.

Hormetic Stressors That Build Resilience

The more demands you place on those systems, the faster they break down and wear out and regenerate humans and living organisms more broadly. But humans are especially good at this.

Have a very have have an incredible, almost magical ability to sense demands on the different systems of our body and adapt to them, not by degenerating, but by actually growing stronger.

Yeah, okay. And as magical and amazing as that is, there is a downside to it, which is the opposite also is true. So what happens if you immobilize muscles in a cast?

Like if you've ever broken a bone, they atrophy. Exactly eight weeks later, you go. You go to the doctor, they saw your cast. You look down at your arm or leg and it's half the size of the other one, okay?

Because the body similarly sense. Well, you know, we only care about survival. I guess we don't need these muscles to survive our environment. They're not being used.

So they're just, an energetic liability. They're just consuming resources, protein and energy without serving any purpose that facilitates our survival.

So let's get rid of them. The same exact principles of growth and atrophy also apply at the microscopic level with our mitochondria. So when they are challenged regularly, they grow bigger and stronger.

They engage in quality control processes, which is what you were alluding to earlier. Mitford and preventing senescence, improving the actual health and function of those systems, growing larger and growing more of them from scratch, model a process called mitochondrial biogenesis.

So you can actually reverse that trend that I was talking about before. You can actually increase the number of mitochondria as well. But if you don't challenge your mitochondria regularly and there are physical challenges that challenge the mitochondria in different systems of the body.

Also think of it this way. Cognitive challenges also challenge the mitochondria of the brain, of the neural circuitry of the brain. In unique ways. And there can even be broken down further from there of specific types of cognitive challenge to challenge the mitochondria in different systems of the brain in unique ways.

And in response to those challenges, those mitochondria adapt by growing bigger and stronger and becoming more numerous. The converse is also true if you live a life lacking in those stimuli and in those challenges to those systems, the mitochondria shrink and atrophy and literally die off, so you have fewer of them.

And as a result of that, you massively decrease your physiological resilience. Yeah. And so you're talking about of

this concept of for medic stressors like exercise for example, you know, if you do an intense workout like I did today, like you probably did today, if I took my blood work right while I was doing that right afterwards, it would look like I had a heart attack.

Massive inflammatory numbers. But, you know, 24 hours later, my inflammatory numbers are really low. You know, I show all signs of great metabolic health, and my system has adapted to create more endogenous antioxidant production, better oxidative stress buffering, you know, and just a better cell to cell communication, all the things that we want for stress, resilience.

And so but I got the right dose. That's the other thing with the hermetic stressors, because there's certainly a limit where you or I could easily overtrain I've been there before, where we're doing too much physical activity, not resting enough, not creating enough, you know, not getting enough of the stimuli like melatonin and, human growth hormone production from good quality sleep to where we're not able to adapt and recover effectively.

And then we're over stressing our system. And so we gotta get the right dose of these stressors like exercise, like learning. You know, which anybody that's a little bit older, you know, you start trying to learn something new, you get pretty easily frustrated.

So, it is a stressor on the mind. And so we got to get the right dose of these hermetic stressors to appropriately boost our resilience factor. And not too much, but also not too little.

Yeah. That's right. So, you know, there's there's a number of principles to extend off of that. But, one thing to understand is that basically too much like, let me put it this way, we have, kind of an abnormal way of thinking about certain stressors, exercise, which we all think of as something that promotes health, is, as you alluded to with your blood test results there, a stressor on the body.

It is a physiological stressor that creates a metabolic waste, that creates a big spike of oxidative stress and even inflammation in the system. It is genuinely a stress on the system if you overdo it.

As you said, if you overwhelm the system with that stress, it will create harm. The the the beautiful thing, though, is that when we engage in types of stress that are biologically appropriate for us because they were historically present in our ancestors over, countless millennia, what happens is we are uniquely, well, well adapted to, creating adaptations to that, that stressor that actually make us stronger.

Okay. And this, this is a distinction between certain types of stressors that are biologically appropriate and were present for the human species for a very long time, that we are accustomed to, versus certain types of stressors like, let's say, lots of the modern toxins in our environment, that we are not well suited to adapt to, that we, that we have enormous difficulty transforming from something bad into something good.

Exercise is a stress that we can transform from something that is, in the immediate term, something bad or potentially bad, into something. Over time, when we engage in it consistently and when we engage in it at a dose, as you said, that is appropriate for our individual capacity, which differs widely between individuals.

When we get that dose right and we go just a bit outside of our comfort zone, just above a slightly above our current capacity, we stimulate transient harm, basically.

But that transient harm is transformed into signals that make adaptations that, in the long term, make us stronger, healthier, and more resilient to future exposures to stress.

Yeah, absolutely. And that's this idea of horror medic stressors. And there's a whole number of different for medic stressors, exercise being probably the the number one example that people understand.

But learning like you mentioned, that's a horror medic stressor in our society today. You know, a lot of people are doing things like cold plunges, right?

Getting cold exposure. There could be, you know, certain types of breathing, like breath holds or, you know, just box breathing and things like that that are somewhat of a horror medic stressor as well, because we're being exposed to more carbon dioxide.

You know, so many people are short, shallow breathers. And I know you have a whole training on that. And so we have fasting as a it's definitely war medic stressor.

Right. Our ancestors would go because they didn't have pantries, right. So they would go, at times, long periods of time without without consuming food.

And their body was able to adapt to it. And so time restricted feeding or fasting strategy that that can be a hermetic stressor that, if done in the right dose, can make us more metabolically fit and stronger, more might, you know, obviously help increase the quality and quantity of mitochondria.

So we have all these types of war medic stressors that can help prime us for resilience. So where do you recommend people start with, you know, some of these different areas that they can focus on.

Yeah, there's there's so many you mentioned a good list there. I would add, sauna exposure to that list. Heat. Yeah. Another aspect is actually phytochemicals.

Very common, extremely wide spread misunderstanding is that most of the, the beneficial phytochemicals, are actually not antioxidants as most people think they are.

They're actually xeno or medic stressors or xeno for meetings, and they stimulate a low level oxidative stress that is transformed. Much like exercise and many of the other stressors, transformed into beneficial adaptations.

So the spike in oxidative stress is actually transformed into an adaptation of, of bolstering and building up what's called the, the the antioxidant response element, which is our internal cellular antioxidant system.

So the more you engage in these types of stressors, and really exercise, breath holding, sauna exposure, cold exposure, all of these actually create oxidative stress, which is something that we all, have been taught in most circles to think of as a bad thing.

But actually, interestingly enough, well, I'll tell him I'll tell an interesting background story related to that. So, about 15 or 20 years ago or so, researchers actually decided to study this, and they what they did was they they recognized that exercise had a whole bunch of health benefits associated with it.

Practical Takeaways and Closing Thoughts

At that time, of course, it was already known that exercise was very good for us. That helped prevent, disease and and so on. But it was thought at that time that it's really unfortunate that exercise also creates this big spike of oxidative stress of free radicals and that these free radicals are damaging us.

So what if we take antioxidant supplements in tandem with exercise? So we get all the all the good stuff from exercise, all these benefits, reduce risk of so many different diseases, but we eliminate the downside of exercise, which is the these free radicals, this oxidative stress.

And these researchers found something unexpected in these studies. The more that they supplemented with antioxidants vitamin A, C, E, things like that, before, during or after exercise, the more that they actually reduced and canceled out and inhibited the metabolic benefits of exercise, because it turns out that part of the adaptations to exercise, a big part are actually adaptations to the oxidative stress induced by exercise, that oxidative stress is actually a signal to grow that internal oxidative antioxidant system, redox system bigger and stronger.

So if you take exogenous antioxidants that reduce the oxidative stress, you reduce the signal on your internal antioxidant system to grow stronger. And it turns out the oxidants are actually a vital signaling molecule for

mitochondria themselves.

To detect that, there is a need for more, increased bio energetic capacity. So all that stuff I was talking about before about mitochondrial growth and biogenesis actually depends on oxidative stress signaling.

Mitochondria have to detect the presence of oxidative stress, which is essentially a, a signal that is that is, translated by them as, oh, we're being overwhelmed.

This this stressor is exceeding our bio energetic, production capacity. So let's adapt to it. To prevent damage, oxidative damage from future exposures to the stress by growing bigger and stronger so we can produce more energy.

So we can handle this bio energetic demand on the system in the future. So, you know, those are all wonderful elements. There's, there's a number of psychological aspects to this story as well.

We create psychological adaptations to mentally difficult things in the same way that we create, and the psychological as well as neurological, actually at the level of the brain, and very much the same way that we create, physical adaptations and cellular and biochemical adaptations to more physical stressors.

So cognitive reserve capacity being one of them. But there's actually many other dimensions of that as well. So the actual resilience to stress is, great.

Is a neurally mediated in large part, capacity. Like, what is your psycho emotional reserve capacity? What is your level of resilience to handle psychological and emotional stress?

Courage, willpower. These are also neurally mediated capacities that are trainable in much the same way that, muscular strength is trainable, via lifting weights.

Yeah, this is really good stuff. I mean, we can go for another hour on this. But what I will say is that I know the listeners got a ton of value out of this.

This interview here. And, guys, you can check out Ari and all his podcast, his programs, his supplement formulas, Energy blueprint.com. I know he's got a great program on breathing.

Also one on gut health, and he's got a great book as well, a couple great books, eat for energy, How to Beat Fatigue, supercharger, mitochondria for all day energy, talks about the phytochemicals, talks about time restricted feeding all the different.

A lot of the things that we discussed here just recently. And he also has the ultimate guide to red light therapy as well. So some great books are is, you know, one of my favorite people in natural health space to talk to you about these ideas.

And I hope you guys get a lot of value out of this. Are you any last words of inspiration here for our audience? I would say the the, the big principle that I want people to realize that really is an extension of everything that I've talked about here, is to realize how much of your physiology is malleable and plastic, and as a function of your behaviors, and you are not as, so much of the medical narrative wants to, to push on you sort of just a victim of biochemicals floating around in your body.

The biochemistry that you assess on blood test is hugely a function of the structure and function that you have built, that you have built in different systems of your body.

And the biggest key to health and disease prevention and energy and longevity is building those capacities. I love that, Ari. Always a pleasure, my friend. Be blessed.