Trigger Autophagy Without Fasting – Dr. Elizabeth Yurth with Dave Asprey – #773

Announcer:

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Dave Asprey:

You're listening to Bulletproof radio with Dave Asprey. Today we're going to talk about something that has a name that you probably aren't going to like. It's called Spermidine. Yes, it comes from, or at least was discovered in that which it sounds like. If you've read my anti-aging book, Super Human, I talked about my quest to obtain Spermidine. No, it's not what you ... There's so many jokes we could make right now, and we're not going to make those, but it turns out it's been incredibly difficult to get, and when I wrote the book, you couldn't get it, other than as a research chemical.

Recently it has become available, and it has all kinds of interesting effects on your health, on your longevity, and it's something I wanted to talk about, but I felt like I couldn't share it with you guys. The only way to get it was to illegally import a type of probiotic from Japan, which is what I did for Super Human. We can do better than that. That's what this episode's about. Our guest is Dr. Betsy Yurth, and she's doing research with Spermidine just as an extract, as a natural form you can get, and what it does for aging, for various health conditions.

She's a physician who's run the Boulder Longevity Institute for more than 15 years, and an orthopedic doctor, and she's a long-time member of the American Academy of Anti-Aging Medicine. This is the people who kind of created anti-aging medicine. It's actually where I met my wife many, many years ago. She works with a company called Longevity Labs that has introduced Spermidine for the first time into the U.S. market, which is really cool.

Before I even formally welcome her to the show, you guys are going to want to know, you can to Spermidinelife.us/dave, you might want to write that down, Spermidine, S-P-E-R-M-I-D-I-N-E life.US/dave, and they'll save you a bunch of money on your first purchase. You have to use code dave25, but I want you to know that because when you hear this episode, you'll know why I've been questing after Spermidine for the past five years, but I just couldn't get it, and now I can, and I'm doing this every day, and I have been ever since I got my first bottle. I want you guys to know this up front. You can save some money. Betsy or Dr. Yurth, welcome to the show.

Dr. Betsy Yurth:

Thanks Dave. Actually, I'm really excited to be here. I've been a long time listener of your podcast, and follower of some of the things you've promoted, so I appreciate you having me on.

Dave:

It's rare to find a doctor who knows about Spermidine. All the jokes we could make here. How did you first get into Spermidine? It's like I don't really know here. I'm not going to do that, but I am a seventh grader at heart.

Betsy:

Yeah, most men are.

Dave:

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Okay, fair point. Now, how did you discover Spermidine, or how did this become an area of focus for you, because longevity medicine, there's so many places you could go. Why here?

Betsy:

Yeah, it really is interesting. I've been in [inaudible 00:03:14] since it was a little tiny group, and it transitioned me from disease-based medicine, as you know, into more of a functional approach to medicine, but I think what we've seen now is that over the past few years, even that is becoming a little bit of an outdated approach. Thinking about systems oriented medicine may still be too simplistic. What we're really finding is you've got to get back down to the cellular level.

A good friend of mine, Dr. William Seeds, who's also an orthopedic doctor out of Ohio, but is a brilliant, brilliant mind, particularly in the peptide space. He is a pathways guru, and really learned everything. He knows everything about cells. I mean I never thought I'd have to relearn the Krebs Cycle and oxidative phosphorylation, but you really do have to relearn all that to really practice medicine.

He's been kind of touting this to a group of us who have been his kind of followers for a while, and he formed a group called Seed Scientific Research and Performance, or SSRP, and took a small elite group of physicians across the US. There's 25 of us who are masterminds who are now studying more cellular-focused medicine. He always seems to be about two years ahead of the curve in everything he recommends, and a few years ago started looking at what's called the Polyamine Flux Pathway in cellular medicine.

At that point, we were talking about Spermidine, and this was, I think, two years ago now, and I, like you, was like, "Oh my gosh, this is the answer to a whole bunch of problems," because it worked at very, very base level in fixing the cell, and I couldn't find it. I'm like you, I didn't have the connections to get it from Japan, and I, like you, was like, "Wow, you can buy it as a research chemical."

It was funny, I don't know if you experienced this, but you got online to even buy it as a research chemical, because as you know, sometimes we do that, it was like, "Make sure you wear glasses, and don't touch it with your hands."

Dave:

Yeah.

Betsy:

It was like, "Well, that doesn't sound like something I want." I actually was calling the company Spermidine LIFE in Austria, and I was trying to get ahold of people, and they wouldn't send it, and couldn't get it. Then, lo and behold, at one point when I'm contacting them like, "Oh, guess what? We're actually coming to the US." I'm in Boulder, Colorado and they actually opened up in Denver, Colorado, so it was this fortuitous kind of meeting, and I was like, "Thank God we can finally get this."

It really is one of these supplements that it's almost too good to be true, and as we talk about it, I think probably the hardest thing about promoting Spermidine is really quite frankly that it really does do everything. When you look at the snake oil does everything, it sometimes seems like it can't be real.

Dave:

One of the things that's interesting, you talk about cellular medicine, and I'm a systems guy, that's my background in computer science and all that, but I ended up going so deep on the cell when I wrote Head Strong, which is a book about mitochondria, and what they do in the cell. I'm like there's all these other cell organelles and it turns out cell membranes are the thing that works, and when those work

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better, almost every bio hack I've ever talked about, changes mechanisms in single cells, and then has a network affect after that, so you're kind of going foundationally. What does Spermidine do in cells that makes it such a broad spectrum thing?

Betsy:

I mean you're exactly right. I just gave a talk, so I'm of the belief that probably everything, every disease process, probably is going to come back down to mitochondrial health, honestly. I just gave a ... We just did a teleconference that was a benefit for the Leukemia Lymphoma Society last week and my lecture was all about mitochondrial health when you look at cancer. It's very interesting, we always think about cancer, okay it's genetic, these genetic mutations, but actually if you take a normal cell, and you add a diseased mitochondria to it, a cancer mitochondria, you create cancer.

If you take a diseased or a nucleus, or a cell that ... the cytoplasm of a cancer cell, and you add a mitochondria that's normal, you'll get rid of the cancer, so we really know that mitochondria are a key player here. Really, where Spermidine works, it works on, at that very base level, in improving that oxidative phosphorylation pathway. It's really working on a couple places. Number one, on helping autophagy, and you speak a lot on this because we know one of the main ways to get rid of bad cells, or have cells to repair themselves is fasting, right?

Right now, we know there's really probably a few mechanisms to help cells to get rid of all the bad cells or to kill themselves off, or recycle the bad parts. One is to reduce calories with fasting. Two is probably to reduce some proteins like methionine, so eating a lower protein diet periodically and three are things like rapamycin. Rapamycin is wrought and used a lot in functional medicine, right, but it's wrought with some difficult issues. It reduces immune function. It's hard to take. You can have a lot of side effects.

Dave:

Yeah. Now might be a bad time, just to break in for a sec there. Now might be a bad time to be doing cycling rapamycin in the middle of a pandemic because I've noticed immune suppression from it as well, so for people who are listening saying, "Rapa what?" There's been a few episodes like with David Sinclair where we talked about that. It's an anti-aging thing, but maybe one to hold off on for a few months. Aside from rapamycin though, you got into the cell, and you said, "All right, what's going on here?" Spermidine, what's it doing in the realm of fasting and all of that?

Betsy:

Just like fasting, it's going to increase autophagy. It's going to help get rid of the bad parts, the bad mitochondria. It works on increasing what's called [inaudible 00:09:09], which is one of the pathways that we know helps get rid of destructive mitochondria. When we look at our bodies, our bodies are really designed to heal. When you look at damage to mitochondria, which is all oxidative stress, you eat poorly, or you are outside in a bad environment, or you're sick, or you take some kind of medication, what is that doing, or you have cancer, what is that doing is it's changing the oxidative phosphorylation pathway.

Remember that's the pathway that's making ATP, it's producing energy. If you now start forming too many free radicals, those free radicals start doing cellular damage. We can take antioxidants but really, if you just pound the body with antioxidants, when you use that oxidative stress, you're actually shutting down one of the mitochondria's ability to heal itself. Where we see the Spermidine work is at a very, very base level to correct the autophagy to get rid of those bad mitochondria so that now we don't have, we're not being overwhelmed by reactive oxygen species.

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We actually will start to recycle the bad parts of the cell, and start with a new cell point. It seems to do a whole lot more than that as well. For instance, in the heart, it actually increases the number of mitochondria.

Dave:

Wow.

Betsy:

Yeah, so we actually see marked increase in mitochondria. It actually in the immune system ...

Dave:

What percent?

Betsy:

I don't know the exact percentage that mitochondria were increased, but it was substantial. When you look at the immune system, remember we have sort of good and bad pieces to our immune system, so in the immune system it increases the M2 macrophages, which are our anti-inflammatory parts of our immune system, so we know that it helps immune surveillance so that now if we start getting damage to cells that could lead to cancer, we've improved immune surveillance.

We know that it actually decreases some of the inflammatory cytokines like tumor necrosis factor-alpha. That links to things like osteoarthritis. It's doing a whole host of things probably because it's working at that very, very bottom level to restore those normal mitochondrial oxidative phosphorylation pathways to stop producing so many reactive oxygen species.

I don't know how many of your listeners are taking ... they're pounding antioxidants, right? When you're doing that, remember when you produce these reactive oxygen species, your mitochondria sends a message to the nucleus. That nucleus responds by sending a message back to the mitochondria to basically start getting rid of these damaged proteins. If that doesn't happen, if we don't up-regulate mitochondrial peptides, and we don't send these messages back for what's called an unfolded protein response, if we don't do that, then the cell becomes sicker, and sicker, and sicker.

Those damaged mitochondria produce a lot of toxic substances that damage things around it. If we go back to Spermidine's base of correcting, recognizing, and getting rid of those bad mitochondria, we stop that whole process. It's really working at a very bottom level, and working in ... We probably don't even have it quite figured out. It's working on so many pathways to reduce reactive oxygen species to reduce, to improve the immune health, to reduce the inflammatory cytokines that we know are initiated in these disease processes.

Dave:

If it's a fasting memetic, can you take Spermidine instead of fasting?

Betsy:

That's a good question, right? We went through that with other things like resveratrol, which we thought were fasting mimetics too, and probably are to some degree. Does anything substitute for fasting directly? I don't know the answer to that. I think there's a lot of people who would like to say yes, that we can take a pill instead of having to fast because fasting is hard. I think that when we look, that

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maybe. The answer might be maybe. I think the problem is what is the dose that would really have that same effect.

We don't know that yet. We know there's a maintenance dose that's very healthy. We know that higher levels of polyamines are healthy. We use very high doses of Spermidine sometimes in our patients who have disease processes that we want to treat.

Dave:

How high?

Betsy:

You know, the question is how high can you go? I don't know if I'm going to answer that, but you know I think the question is how high can you go in patients and still be safe? I think it depends on some of the markers that you're following on people. We're following a lot of markers, but when I do regenerative procedures on people, one of the things Spermidine does is actually increases stem cell activity, so if I want to throw stem cells into a knee joint, I'm going to always follow that with using a relatively high dose of Spermidine for a six-week course.

I think there's a maintenance dose that's probably really good, one gram daily, and then there's probably higher doses that are going to have more beneficial processes for disease, and can we get to a dose that would have the exact same effect if I fasted for 48 hours? I don't know that. It would be nice.

Dave:

Probably a good idea to take it during a fast?

Betsy:

I think it would accentuate the fasting benefits, yes.

Dave:

It would? Okay.

Betsy:

Mm-hmm (affirmative) because it would offer more protection, more cellular protection.

Dave:

I have a new book called Fast This Way.

Betsy:

Right.

Dave:

By the way guys, this is a plug. If you haven't pre-ordered Fast This Way, it's because you're a bad person and you don't like yourself. Just kidding. There's a whole section in it on fasting supplements, or what should you take during a fast to make it work better, and not take, and I didn't put Spermidine in there because you couldn't buy it when I wrote the book. Now that it's already at the printers, but hasn't been

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sent out yet, I can't add this otherwise this would be on my list of things to take. We've always eaten some Spermidine though, right?

Betsy:

Spermidine is in our diet. It's in soy. It's in mushrooms. It's in those aged smelly cheeses like Roquefort. It's in soybean peas, mushrooms. Yeah, it's in our diet. In fact, one of the theories is that one of the reasons the Mediterranean diet is so good for us is because it has a high polyamine content, so it is in our diet. Particularly in some of the Asian populations, they probably eat more of it than we do. We do know that the higher amount of polyamines like Spermidine that you eat, that they've looked at polyamine intake and longevity, and we know that there is a parallel line between polyamines that you eat, the longer longevity you have, especially if you start at an early age, so this is something you'd probably want to start very early, and kind of continue on a regular basis. You can get it from foods. It's mostly, again, in the cheeses, mushrooms, vegetables.

Dave:

In wheat germ, right? That's the number one source?

Betsy:

Wheat germ is one. Wheat germ is one of the best sources for us to get it, at least from extracting it, and there's only certain types of wheat germ that it comes in in very high amounts. A very specific type of wheat germ, and it has to be extracted in a very careful fashion, which is why I think it was so hard to get. It's actually extracting large amounts of it out of wheat germ. You need a very specific type of wheat germ. You need a wheat germ that was GMO free. You needed to do an extraction process that actually didn't damage the Spermidine as you were extracting it.

I think that was one of the difficult things because if you look back, you can find research on Spermidine dating back a long time.

Dave:

Oh yeah.

Betsy:

There's an article in 2003, right? Why did it take so long to get here?

Dave:

Those are the ones that were ... Those are the articles that informed my work on the anti-aging book. I just wanted to highlight there's all these things that we know that we can do that people aren't doing, but one of the concerns I had is the Spermidine LIFE stuff that I'm taking, it does come from wheat germ because it's like the richest source they could find, and I know it's carefully sourced. Do you see patients who have gluten problems having any issues with it because it does come from a wheat-based substance. Is that a thing?

Betsy:

It's an interesting question. If you read the bottle, it does say if you're celiac, not to use it, but I do use it in my patients, and the reason is because if you look, the polyamines actually are what we call tissue transglutaminase inhibitors, and we know that those TTG, those tissue transglutaminase inhibitors, will

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prevent conversion of the gliadin, it was called deamidated gliadin. The deamidated gliadin is what creates the immune response in your celiac patients.

Actually, an immune response, not even just in celiac patients, but in just your gluten sensitive patients, but also maybe those deamidated gliadins may actually have a link to some diseases like Parkinson's and things. Because the polyamines, all of them, are TTG or tissue transglutaminase 2 inhibitors, we may actually prevent converting it into the bad form that creates the antigenic response in your celiac patients.

I have a number of celiac patients that I have on Spermidine probably from the products, if you read the back label, because it is a wheat germ product, they say don't use this if you're gluten sensitive, but from my experience as a physician, I will certainly cautiously use it.

I have had a few people even who aren't gluten sensitive who had some stomach issues, and I don't know exactly why that is, but I have a number of celiac patients who have tolerated very well, and actually we do think the tissue transglutaminase 2 inhibitors may actually be a way to help treat celiac patients, so it may actually have some very good benefits partly because it is so immune regulating and lowering those bad parts of the immune system, up-regulating the good parts of the immune system, so it naturally would be fine.

I would use it with the guise of working with a physician who understands Spermidine. There's not very many out there.

Dave:

Okay. As someone who's pretty sensitive to gluten, [inaudible 00:18:57], and I just do not feel good. I get massive cravings when I eat it. I am taking four SpermidineLIFE capsules a day, two in the morning, two at night, and I don't have any of the gluten style issues from it, and I also know a guy who has formulated many supplements in my life.

You put things on the label so you can either pass regulatory muster or so you don't get sued. For instance, almost all supplements say don't give it to anyone under 18, and that's just there for insurance companies, even though I kind of think kids need nutrients, but that's why you always have to do your own research if you're in your teens, and deciding to supplement, and you can also do great harm with them, so I don't want to say that it doesn't matter because it does matter, but it's one of those things where if I was formulating this I'd say, "Hey, if it comes from wheat, I'd put on there just in case there's one person who's really sensitive." To my knowledge, I haven't met anyone who's had a problem, and I've been talking about Spermidine [crosstalk 00:20:00].

Betsy:

Yeah, you're right. Like you, I take four a day. I'm very gluten sensitive as well, and I have no issues with it at all. I have [inaudible 00:20:08] celiac patients who I have on it as well, but again, you're right, as we know working with the government's not always easy.

Dave:

If you had a patient you'd just done a bunch of regenerative procedures on them, and you want them to heal faster, do they also take four a day, or do you kick it up a little bit?

Betsy:

I think four a day is a really reasonable dose. One of the things that happens is No. 1, expense. It comes expensive to use high doses and you're already ... Some of these people doing very expensive

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procedures on them, so typically what we'll do is four a day in those patients. I do have a few patients we've gone to higher doses on who are very sick people.

Dave:

Like 10 a day, or like 100 a day? Just [crosstalk 00:20:46].

Betsy:

No, not like 100 a day, but ...

Dave:

Like 10 a day?

Betsy:

I haven't gone up to 10 a day, no, but you could probably very easily get to six a day.

Dave:

I'm going to do 10 tonight and see what happens.

Betsy:

I think when you look at the safety, I mean this is a natural ... Polyamines are naturally in our diet. It would be like saying, "Can I eat too many mushrooms?" I don't know, can you? I guess it depends on the type of mushroom, but it is really ... This is something that's naturally in our diet. We know that higher amounts are better in general for people. We've equated that. We've looked at that. There are now so many studies on Spermidine, looking at it. At least in animal models there didn't appear to be a ceiling dose on it that caused significant side effects.

I honestly think that it's probably really, really safe. I do think the source is important. One of the things about the Spermidine LIFE that's taken out of wheat germ because there are other Spermidine sources, is that it's sort of like cannabis, is that it's kind of a spectrum, it's not just the Spermidine, and that wheat germ extract also has a little putrescine and a little spermine, so it actually has kind of the whole spectrum. It's got the spectrum of polyamines in it. It's mostly Spermidine, but when you have that whole spectrum, it probably is going to be safer than to pound your body with one thing only.

Dave:

Sort of whole foods based ...

Betsy:

Exactly, so it's a little bit more whole food based approach. Just like if you look at just taking CBDs or just taking THC and not having a full spectrum hemp, there's probably differences in the way it's going to react in your body, right? The same thing is true with Spermidine. It's one of the reasons that we've really appreciated Spermidine LIFE product.

Dave:

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Can you talk about putrescine for a minute? I wrote about the biogenic amines in The Bulletproof Diet way back like 10 years ago, and generally it looks like two months putrescine is not good for you. It's called that because that's what rotting corpses smell like, and histamine is another biogenic amine. That's a problem. Histamine, why am I getting [inaudible 00:22:54], why am I tired, and why do I have cravings after my food? It's like those three-day old leftovers with fish and soy in them probably were a trigger. Not all biogenic amines are good. Tell me about putrescine. Tell me about the other biogenic amines.

Betsy:

Putrescine basically converts into Spermidine, and then Spermidine into spermine. If you overwhelm parts of that pathway, are you doing harm, and I think that's where just taking Spermidine may actually have some issues too. You may overwhelm pathways. You can very easily, with putrescine it can take a different route, and it can become a very toxic element, as opposed to the Spermidine, it can't backtrack the same way. Putrescine which right, when you go even by plants that are rotting, when you go by plants, and you have that smell like I'm not very good with plants ...

Dave:

That putrid smell.

Betsy:

A really putrid smell, and that's really where it got its name. It's actually from rotting meat. We do get, if you eat bad meat, you'll get putrescine. You can overwhelm that pathway and then it will go into much more toxic metabolite doing a whole lot of damage. That's why you really wouldn't want to just eat putrescine even though it will channel into Spermidine into spermine, you theoretically say, "Okay, it's a lower level pathway." The problem is it can take a whole nother route when you overwhelm that pathway.

That's where I think Spermidine becomes a much safer choice, not to mention you probably don't want to eat something that smells like rotting meat, but that's really the difference in why these biogenic amines, they're going to have different ... If you have to go back to that pathway, back to that cellular pathway, and watch all the different pathways that can be taken, and putrescine can very easily alter when you overwhelm that pathway and not go the way we want it to.

Dave:

A guy who I would call the grandfather of the carnivore diet, whose name I could not pronounce, but it's like Andreas something or another, was an advocate of an old practice from something he got from Inuit people where they would hang their meat until it spoiled, and then they would eat it, and they'd feed it to their sled dogs. He was telling people before he passed away, "Take your meat, put it in a jar on the counter, let it sit there for a couple weeks, and then eat it." No, I have not tried that. There are a few things I won't try, but that just cannot be good. I'm imagining he was getting all sorts of crazy levels of biogenic amines from doing that.

Betsy:

Right. Right, and some good, right. Maybe he saw some of the benefits, at least in some people. Again, that goes back down to what are your pathways doing? In a perfect world, the putrescine would go into Spermidine, it would go into spermine. You have all these advantages. The problem is that not all those are perfect, and number two, it depends on how much you're taking in.

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Dave:

Yeah, and a lot of other people on diet are like, "Oh, I'm pretty sure I'm detoxing because I have bumps all over my body and I feel high."

Betsy:

Right. Right.

Dave:

I'm pretty sure [crosstalk 00:25:42].

Betsy:

It's a lot, yeah.

Dave:

That's just me. I was a raw omnivore for a while. I'd eat raw meat, but not raw spoiled meat. There's that. We know that gut bacteria can make Spermidine as well. Do you have an data on if you're not taking that weird probiotic from Japan that I wrote about, if you're not doing anything in particular, how much Spermidine do we make onboard just from eating meat?

Betsy:

We definitely do. If your gut microbiome is really healthy, and there was actually just a study that just came out pretty recently and I think I read it maybe two months ago that actually looked at what happens to the gut microbiome when you're warm versus when you're cold. In a hotter climate, the gut microbiome actually made more Spermidine, so the gut microbiome was erred to the side of making more Spermidine and actually we saw the same thing [inaudible 00:26:38] actually on osteoporosis that they saw that people living in warmer climates had less osteoporosis than people living in colder climates and equated it back to a difference in the gut microbiome and this gut microbiome making the higher levels of Spermidine even in diets that had very little intake in Spermidine.

It does appear that you can make pretty good amounts if we have perfect gut microbiome. The problem is that most of us don't, right, and two is that it appears to be a very specific concentration of some certain bacteria that will help make that Spermidine.

Dave:

Wow.

Betsy:

If you have higher level of Spermidine, it will improve the gut bacteria that make more Spermidine, so actually it becomes sort of a cycle, which is why probably you might be able to say, "Hey, I can maybe not have to continuously use high dose Spermidine, but go on a high dose for a while, and then take lower doses, and go on a high dose for a while." I know you, like me, I believe in cycling things a lot, right?

Dave:

Yeah.

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Betsy:

Not stay on the same diet. I think the carnivore diet, it's not something you want to stay on all the time.

Dave:

[crosstalk 00:27:54].

Betsy:

Then, you're going to have to [inaudible 00:27:54] all the [inaudible 00:27:54]. You do it for a month, you do it for six weeks. I'm a big believer in six to twelve week cycles of things, right? Lots of times what we can do, what we'll do is we'll put you on a higher dose of Spermidine for six to twelve week cycle, depending on what their health is like, and then we'll put them on a maintenance dose for a while, and then maybe hit them again with a high dose.

Theoretically what you might be doing then is improving the gut microbiome to an extent where they're making their own higher levels for a while. You've kicked the body back into gear. Remember the other thing is this whole autophagy piece is that when I've gotten rid of all of the bad stuff, when my body has now reset, then I'm going to be in a state where I can now ... All those pathways get back in order. I'm not producing so many reactive oxygen species. I'm not overwhelming these pathways that my body helps deal with all these bad things.

If you can cycle those for higher doses for a period of time, and then go to lower maintenance doses, I think it's probably a really ideal thing. You go through a very ... just like we used the rapamycin, or quercetin, or fisetin in terms of autophagy, go hard for a period of time, and go to a very maintenance level. Probably one of the pieces there is just restoring gut microbiome, but also getting rid of all the bad crap.

Dave:

I love it, straight up. Get rid of the bad crap. In fact, doing that first might be a ...

Betsy:

Right.

Dave:

... good piece of advice.

Betsy:

Honestly, that's a really important thing, right? Before you start doing anything that's up-regulating, get rid of the bad stuff. As an orthopedic doctor, all this oh does regenerative medicine work? Do stem cells work? If you're a traditional orthopedist, lots of times like this stuff doesn't work. There's no proof of it. Well, if you're in a horrible state, and you basically have overwhelming reactive oxygen species in all your cells, including in your cartilage, then I throw a bunch of your stem cells in there or platelet cells in there, what's going to happen? Nothing. You're going to kill off those cells and you'll be back to where you started.

We go through a really intricate part when we're treating patients in a regenerative fashion of using things like Spermidine in a high dose, going through a phase where we kill off all the bad stuff, and then put in good stuff. Very interestingly platelets have a whole bunch of Spermidine in them too, so

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actually one of the ways platelets probably is working is upbringing Spermidine, which we know is important for cell differentiation.

Then, you put in the platelet cells, or stem cells, or whatever your passion is, and then follow that with a dose of Spermidine again for a six-week course, and our outcomes are dramatically better by doing things like that with people.

Dave:

Wow. I'm going to ask an inflammatory question here, and I'm going to preface it by saying anything that you do that makes your cells healthier is going to make you more resilient to everything. The reason I'm prefacing it is now do we have any data about Spermidine in COVID-19?

Betsy:

Actually, a study pretty recently that came out on Spermidine and COVID-19, and I don't want to have this pulled off the air but ...

Dave:

We're not talking about treating, diagnosing, or curing that. We're just talking about being stronger. What does the study show?

Betsy:

What it did was, again, improved the ... Remember what happens when ... There's a couple of things that happen when COVID goes awry, and one of the big things is we know there's this cytokine response. That bad cytokine response, these inflammatory cytokines start causing this cellular destruction and that's why people go on to have cardiovascular damage, and strokes, and kidney damage is because now you've damaged the lining of the blood vessels because of these cytokines that have appeared in a response to the COVID.

We know that Spermidine, again we saw that in the osteoarthritis mouse study is that it markedly reduce a lot of the inflammatory cytokines that we see elevated, like tumor necrosis factor-alpha and interleukin-6 ...

Dave:

IL-6.

Betsy:

And IL-6, right.

Dave:

There you go. That's the one.

Betsy:

And it up-regulated the M2 macrophages, which are your good anti-inflammatory macrophages that help get rid of bad things. The other thing it could be used for is again, remember that to form a normal immune response, to have normal immune surveillance is that you basically have to have this balance between the anti-inflammatory and pro-inflammatory side of our immune system. If somebody is so

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inclined go get vaccines, this is definitely going to enhance the vaccine efficacy as well because you're going to be able to respond in a much more appropriate fashion to somebody putting a new antibody into you.

Dave:

Could it maybe lower risk as well? I know this is entirely hypothetical.

Betsy:

I think it's definitely going to lower risk because again when you get your body into an immune-healthy state, as we all know, that's why higher dose vitamin, anything that gets our body into an immune, healthy state is going to make us a lot less likely to get COVID and get sick. If I have lower reactive oxygen species, that's why obesity is a risk factor. That's why cardiovascular disease is a risk factor, it's because those guys have very high levels of reactive oxygen species.

Their bodies are in a very poor state to recover, so you get some little infection and you have a horrible outcome. By down regulating the reactive oxygen species, up-regulating the anti-inflammatory macrophages, the M2 side, reducing the inflammatory cytokines like IL-6 and TNF Alpha, you're in a perfect state to be able to fight this disease, or not get it at all.

I'm not very afraid of getting COVID. I do all sorts of things to keep my immune system healthy. I think that unfortunately we're focusing so much on isolating ourselves and everything, and not just getting healthy.

Dave:

If you're not afraid, you're not a good person. Just remember that.

Betsy:

Yeah, you're right.

Dave:

Sorry, you have to look at your individual risk, not average risk, and all that kind of stuff. We don't have to get all political. Wait, I thought this was science. Nevermind. We won't even go there, but I appreciate you saying that you don't have a high degree of personal fear there because that's a refreshing [crosstalk 00:33:54].

Betsy:

I wear my mask, and I'm careful around the people, but I do think ... You've pushed this. It all comes down to people have got to start taking some responsibility for their own health. Like I said, before Spermidine ever makes it to ... before your doctor ever recommends Spermidine to you, it's going to be, I don't know, 10, 20 years, maybe never.

Dave:

No, it's going to happen. I'm doing my job. My job is to make this stuff no one knows about happen faster.

Betsy:

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Right, and that's our goal too. Boulder Longevity Institute, we have a whole what we call Human Optimization Academy. Our goal is to teach the people because you've got, and that's why I love people like you who are out there spreading this stuff because if you rely on somebody, a doctor, to tell it to you, or the drug company to bring you something, you're going to be way behind in terms of treatment, so you need to learn these things. You need to understand these things.

Dave:

I have long considered Spermidine as important as Glutathione, but I couldn't get it. Do you think it's as important as Glutathione?

Betsy:

I think it's more important quite frankly.

Dave:

Wow, okay. That's incredible.

Betsy:

Look at the number of things this does. I think it's going to come back to it's really working right there on that whole inner membrane of the mitochondria on the oxidative phosphorylation pathway to change your metabolic health. Your podcast you did with Jason Fung recently. It's going to come down to metabolic health is a big key player in cancers, and Alzheimer's, and dementias, so if we can restore metabolic health, which is making the mitochondria healthy, and that's where it works so I think it's working a base layer lower than glutathione is.

Dave:

Wow.

Betsy:

It's probably going to be really ... Right now, if you were to ask me is there one supplement, if I abandoned everything else, and that would be hard for me to do, but if I abandoned everything else, this is the one substance that we can absolutely say this is in our diet. It's across every eukaryotic species, right? Every single species, every one-cell organism. Everybody has this, so we know it's critical to life. We absolutely know it's critical to life.

Anything that's preserved for that many species, we know is absolutely critical, so I think that when you look at all those things it's doing, and how important it is, and we have all these studies now that are showing that it's affecting immune health, brain health, cardiovascular health, joint health, you can't really say that about glutathione. That one substance that I would take if I had to take only one thing, it would be Spermidine.

Dave:

We know that Spermidine is protective of the liver. Is this something that you should take if you're going to drink alcohol? I've always told people "Yes, take glutathione," but should you stack glutathione and Spermidine if you're going to have a night of partying?

Betsy:

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It's really actually very liver protective, and that's actually some of the bigger studies that have been done on Spermidine is in the liver. It increases NRF2, so it's very, very, very protective to liver, and actually has reversed liver disease in people. We've used it in patients who have just alterations in liver functions, sometimes unclear why. The liver is such a sensitive organ.

Sometimes to see why the liver, you sort of see elevation in transaminases is a little difficult. You go through eliminating everything they're taking orally, and people aren't drinking, and still have some elevation in liver functions. You can see really nice improvements in liver, so I think it's both protective, but also restorative in liver function. Seen the same thing in kidneys as well. I think it would be a really useful thing.

Like I said, I would take it every day, but I would probably say, "Yes, you're going to go out for a night of binge drinking, don't advise it, but if you're going to do that, then I would at least take a double dose of it, and give some liver protection." Again, is it more important that glutathione? At lease equally important in liver function.

Dave:

Wow. I've known it's an anti-aging powerhouse, and you know about some of the things I just haven't seen, which this is fascinating to me because I didn't know that much about the liver and Spermidine specifically. Talk to me about fat loss and weight loss and Spermidine. What do the studies show?

Betsy:

Brian Kennedy who's in Singapore, their lab just did a bunch of work on Spermidine and fat loss. It's interesting because the way it really appears to work on fat loss is by actually increasing some of the transaminases that are converting fat. It works specifically on visceral fat, so it's actually really, really important for visceral fat, which as you know is the more dangerous fat, and sometimes a very hard fat to get rid of.

Dave:

The fat around the organs.

Betsy:

Yes, fat around the organs, and when you look at these 50-year-old guys who have the dad bods, and the big old bellies, that's a really dangerous fat, but it's also really hard fat, sometimes, to get rid of. What they've found was when they took mice, and they gave them Spermidine, and put them on a high fat diet, that totally protected them from gaining visceral fat. It worked in young mice. It worked in old mice, but it worked really particularly well on that visceral or bad fat. You have white fat and you have brown fat. It's the dangerous fat.

Dave:

That's the fat you can't see around your organs.

Betsy:

Yeah, but most people have ...

Dave:

It hides.

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Betsy:

Yeah, it hides around your organs, but most people who have that big belly, most of those people have visceral fat. It's why we can measure abdominal circumference and make an estimation of visceral fat based on just abdominal circumference, that those people have higher levels. They found that it increases the lipolysis basically by up-regulating these adipose triglyceride transaminases that are moving the fat out, so it was really protective, even though it didn't directly affect in the metabolic status to increase weight loss. It wasn't like it increased metabolism and so your weight was [inaudible 00:40:03], it really was very specific to working on some of these transaminases that converted the white fats, so that was really interesting.

His study was across the board. It was not age-dependent. It was not sex dependent. It didn't seem, even though we know that Spermidine also works on autophagy in fat cells, it didn't actually seem even not related to that, and so there's this up-regulation of all these different transaminases when you look at the fat lipolysis pathways. It was really cool in that realm. Again, is there anything it doesn't do?

Dave:

Wow. There's also some interesting stuff around Spermidine and hair. Can you tell me what's going on there?

Betsy:

It's actually one of the more ... You can view almost any study and I've seen a lot of studies disputed, but nobody can really dispute the hair growth study. It definitely had a marked effect on hair growth, and it's because of its stem cell activities, it's epithelial stem cell activity, so you're increasing basically the number of hair follicles, so you're actually not just ... Hair grew faster. It grew longer, and it increased density. It was pretty marked over, I think, a relatively short period of time, over a six-week period, they saw significant increase in hair growth.

Here's, again, another reason, if nothing else, nobody wants to lose their hair, so that is a reason to take it every day. We also know that the diet, places where diets are higher in the polyamines have thicker hair, better hair, don't lose their hair as much. Again, just another benefit of this drug, or this supplement, not even drug.

Dave:

Should I be popping a cap open and putting it in my shampoo?

Betsy:

You know, I don't know of topically, I mean the hair, the scalp is very good for absorption of things, right? Can you absorb it topically? I don't know that. I don't know if it's too big to get a good transdermal effect, and what you could add it to. I think just taking it orally is really what you want to do because it's really increasing things from the inside out. It's increasing that stem cell production.

Dave:

What was doses required for hair?

Betsy:

Normal dosage of Spermidine LIFE would be two capsules, which is 1 milligram dose.

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Dave:

Okay, so two pills a day is what they used in the study?

Betsy:

Two pills a day, maintenance dose in the study, yeah.

Dave:

Okay.

Betsy:

A lot of the studies, one of the really nice things about Spermidine LIFE is if you look at all the studies, and there are so many studies coming up now. 2020 alone right now, I can think off-hand of about 10 different studies. There's still three ongoing from 2019, long, short-term studies following ... There's a Smart Age Study that's still continuing, looking at brain health. There's so many studies now on this supplement. I would venture to say more than a lot of supplements that are out there, so people are really getting this on their radar.

We have a lot of data now coming, which is nice because we can really look at things now and say, "Okay." Most of the companies that are doing it, or most of the researchers who are doing these studies, are using this Spermidine LIFE product which says a lot, that this is what they've chosen as their research supplement is this product itself. That's encouraging and makes you feel a little bit better about it, that this is the one they're coming to, this is what they're going to.

Smart Age Study, which started in 2017, that was even earlier, right? That was before you and I could get it, well you could. I couldn't. 2017 study, Smart Age Study, took I think it's 100 people who had subjective cognitive impairment, so people who nobody said were cognitively declining, but the people themselves felt like they would, and have been following them now, I think the study just completed, or is about to complete, I think November 2020. It's just about to complete, so they've been following them for three years.

What they're seeing is significant improvements in every level of testing on just this one gram, 1.2 grams daily dose of the Spermidine. In another study that just came out on brain health, it was published this month, that actually measured volume, so brain volume, and hippocampal volume, and shows substantial improvement after just six weeks of Spermidine. [inaudible 00:44:18] dose.

Dave:

Wow. That's nuts.

Betsy:

Yeah.

Dave:

Hippocampal shrinkage is a major problem as we age, and it's one of the markers I track on myself. I'm at the 87th percentile for my age, so I'm holding onto my hippocampus as I age, but six weeks to increase hippocampal size is nuts.

Betsy:

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It's nuts.

Dave:

I did not know about that. Was it humans or mice?

Betsy:

That was on human study, so that was using [inaudible 00:44:43] studies. They'll follow that along. They'll probably continue to get further improvement as time goes on, but again, when they looked at curves of life span in the polyamine intake, if you started early, you could just not lose your ... You and I who started later in life taking Spermidine, we've lost some time, but you can see people regaining, so we're regaining years by taking this supplement. There's really not a lot of supplements out there that have shown that.

Dave:

There's almost none.

Betsy:

There's almost none.

Dave:

For hippocampal volume? I've never seen one, have you?

Betsy:

No. I think there's ...

Dave:

Wow. That's like the realm of hyperbaric and stuff.

Betsy:

There are some peptides I think that maybe have shown some improvement, but they're more difficult to obtain. This is something that's so easy and so safe. Again, we're relatively new to it. We've only been able to get it for, I don't know, a few months now.

Dave:

A few months.

Betsy:

Yeah.

Dave:

There's one other aging aspect. We talked about the hippocampal volume, which blows me away. We talked about hair. What about vascular because there's so much going on. We did a recent episode where we talked about just the lining of the arteries, and how you can protect that. What is the role of Spermidine in protecting or doing anything to our blood vessels and our circulatory system?

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Betsy:

A lot of the studies actually are on the cardiovascular system, and there's a study, it's still ongoing called the Smartest Study that's actually looking at blood pressure, so actually hypertension, treat it with Spermidine. The early results from that are looking pretty promising that it actually is really helpful there, but again, for lowering ... LP (a), which is one of the hard things to treat, so if you genetically have high LP (a), then it's a tough thing.

We've used niacin, but niacin doesn't work all that well, and it's actually hard to take for a lot of people. Might have some other down sides, so the Spermidine actually lowered the LP (a), and this is a group of patients I have a hard time with because getting LP (a) down, we know that that is an inflammatory cardiovascular, or increases inflammation of the blood vessels was accredited to heart attacks and strokes.

Again, we talked about the increase in mitochondria within the cardiovascular system so it may be really that helpful in early congestive heart failure patients because you're going to increase mitochondrial production, and that's going to increase the energy production of the heart of each heart muscle cell.

Again, by just increasing oxidative phosphorylation, decreasing reactive oxygen species, that's going to all be cardiovascular health as well. It's all mitochondria. Remember your heart muscle is one of the biggest producers of energy. It needs a lot, so by correcting that ATP production in the cardiac cells, it's going to be really beneficial. It increased SIRT 1, so that's going to also be helpful in terms of cardiovascular disease.

I think it's kind of, again, hitting each one of those points, but the studies have shown reduction in lipid profile, reduction in LP (a), improvement in stroke volume on the heart, looks like reduction in, again the study's not done yet completely, but at least in mice and human study ongoing, reducing blood pressure. It's hitting almost every aspect of cardiovascular disease.

It's now my go-to. My sort of first-line in my patients who have abnormal lipid profiles, and/or who have any kind of like [inaudible 00:48:08] peroxidase levels, high oxidative LDLs. Those are both stress markers, the reactive oxygen species markers, so if we can reduce reactive oxygen species, reducing all those markers, you're improving cardiac function.

It's now my first go-to on my patients with cardiovascular abnormalities on their labs, even if they have normal coronary calcium scores, everything's normal, if I start to see high elevation Myeloperoxidase or an elevation in the oxides LDSs, my first go-to right now is I'll hit them with a 12-week course of Spermidine, and we're seeing improvements.

Dave:

Wow. This is sounding almost too good to be true except for they're familiar with the research. It's real.

Betsy:

I know. Isn't that the hardest thing though?

Dave:

Yeah. Okay, the other big thing that happens when you age is this tissue loss or sarcopenia, and we see older people, they just have less muscle mass. It's okay you don't have the muscle mass of a body building 25-year-old, but you see a linear decline in Spermidine levels, and a linear decline in muscle as you age. What does it do for maintaining muscle mass?

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Betsy:

We're kind of back in the same place. For bone and muscle, one of the big things is increase in stem cell production, so increasing stem cell production in the muscle, also for bone, which is why it's so helpful for osteoporosis. Those are both loss of stem cells in the muscle. Loss of stem cells in bone is one of things that is now causing that demise as we age. That's probably its big effect is on stem cell production, but again, if I'm going to increase improvement in mitochondria, again loss of mitochondria muscle cells, improving the mitochondria is going to make the muscles more functional.

It will both increase muscle stem cell, so I can build muscle more easily, but number two, increase the function of that muscle so I have better muscle contraction. In muscles, you're aging currency. You need muscle to survive. I really do a lot of weightlifting, and I'm really adamant with my patients that you can't just be doing cardio. We have all these who are just doing cardio, cardio, cardio, that you've got to be lifting weights. You've got to be going strong.

This is going to allow you now, because if I don't have good stem cell production anymore, I'm 70 years old, and have really taken care of myself, and now I'm telling this 70-year-old to go lift weights, they're going to have a really hard time. If I can increase stem cell first by using the Spermidine for a good 12-week course, again maybe a little bit higher level in that elderly patient, it's going to encourage them to be able to go lift a little bit more, go do a little bit more.

Now, if they're continuing to use it, those muscles are going to be functioning better as well, so they'll be able to run faster, lift harder, not get so sore afterwards. I think there's a huge benefit there. I've been using it along with, interestingly, Oxytocin for muscle building. Oxytocin [crosstalk 00:51:01].

Dave:

You have some nice shoulders. I was thinking that ... I can see that you're doing something right.

Betsy:

Yeah.

Dave:

Is Oxytocin nasal or how are you getting Oxytocin?

Betsy:

You can do nasal spray, or subcutaneous injections of it. We'll do that with a lot of our clients, or bodybuilder people because it's a huge anabolic agent, and we forget about Oxytocin as an anabolic agent. You can use Spermidine and Oxytocin, and get really nice ... You basically use the Spermidine on a regular basis, usually a hard course of it, and then on a regular basis, and then you use Oxytocin like right after the workout to get muscle pump, and you'll see really good muscle production.

Dave:

I talked to a bodybuilder once who swore by, this is going to sound funny, like nipple stimulation after a workout to raise Oxytocin levels.

Betsy:

Right, it works in the same way.

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Dave:

Have you heard of this before?

Betsy:

Yeah. It's doing the same thing. It probably can get more Oxytocin by actually taking Oxytocin ...

Dave:

Injecting, yeah.

Betsy:

... but it's the same principal. That's why bodybuilders who work out together seem to get better results than working out independently. It's that socialization that increases Oxytocin as well. Now, what we're all sitting in our houses by ourselves, not seeing people, not socializing, not touching each other, so our Oxytocin levels are probably really low, so I think those Oxytocin along with the Spermidine is a really nice combination for people who want to get more muscle, especially to get older people started or even young people who have gotten really sarcopenic from being sick, or just being unhealthy, it's really a nice thing to get them a little boost.

Dave:

Wow. This is really cool. I had never even thought of Oxytocin with it, and I guess it means I'm going to have to play with my nipples, or you could just hug someone, and since I am in a relationship, you could just cuddle on the couch [crosstalk 00:52:53].

Betsy:

You could hug more, yeah that's right.

Dave:

That's more likely what I'm going to do. What about when people shouldn't take it? Are there down sides to it?

Betsy:

I guess the big question there is cancer. We just don't know yet. It appears to have a very cancer-protective effect.

Dave:

It should, given what it does.

Betsy:

It should, right. There is a recent study in colorectal cancer that showed it to be very beneficial in helping those markers to reduce, but if you think about now if I'm stimulating oxidative phosphorylation, if I'm getting more ATP, cancer cells love energy, right, so am I stimulating some fast-growing cancer cells. I think the same question comes around with like IGF, the growth hormone secreted [inaudible 00:53:39]. It depends on sort of what school you're in.

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I guess the legal answer to that question is probably if you have active cancer, don't use it, but there's probably going to be further evidence coming out to say, "Maybe some cancers it's good for, maybe some cancers it's not good for." I think we've been in the same question with the IGF, the growth hormone [inaudible 00:54:04], things like that. Are they good? Are they bad? It probably is going to depend a lot on what's going on inside the cell.

Dave:

That's a really nuanced and awesome answer. Thank you for that. Anything that increases growth can increase cancer, and this is one of the things where you have to increase your mitochondrial function, which is anti-cancer, and you have to increase autophagy, which is anti-cancer anytime you do something to increase the young stuff that you're doing, but it sounds like, given all the effects on mitochondria, that Spermidine is helping mitochondria, so my rough bio hacker assessment, not being a cancer doctor, or any kind of doctor, would be it's probably okay, but like you said, if we don't have studies on it yet, other than one that says it might be good for one type of cancer.

Betsy:

Right. I think it's going to be ... Here's what I think you're going to have to go back to is it's why antioxidants are not necessarily good in cancer. You want some oxidative stress, so I actually think [inaudible 00:55:06] going to come out to be very homeostatic. It's going to actually get things back to the way they're supposed to. It's why I'm not a big fan of pounding antioxidants all the time. I think that that is probably a bad thing.

I think because this is so homeostatic, it probably is going to prove to be beneficial, but right now, the kind of rule of thumb is we don't know.

Dave:

One of the things I wrote about in Fast This Way, again you guys are seeing my subtle plug for this, is that taking antioxidants in the middle of a fast is probably not a great idea unless you're dealing with excessive inflammation because you want a little bit of stress on the cells, right?

Betsy:

You want the reactive ... Right, you want that stress. That's what's kicking everything up.

Dave:

Spermidine is not an antioxidant, so you can take it during a fast, and it probably will improve a fast is what I'm guess here. I'm certainly doing that during ... I take it in the morning during an intermittent fast.

Betsy:

Yeah. I take it twice a day when I'm fasting, and doing a longer fast, but again, remember it's working ... Whereas antioxidants are working once you've created these reactive oxygen species, you're taking the antioxidants to help eliminate them. Spermidine's not doing that, so we want these reactive oxygen species.

That's what actually codes mitochondrial peptides, mitochondrial peptides like SS-31, and Mot s.c. those are mitochondrial peptides is what actually help us to heal and recover, so if you don't have any oxidative stress, you're not going to get the recovery and the autophagy, and so it's working back in

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the layer before the antioxidants, and that's why it's going to be so beneficial is you're not blocking that oxidative stress, you're giving a nice homeostatic approach to it.

That's why I think it's going to pan out to be much better option across the board for everything over antioxidants because theoretically, my body, I should not have so much reactive oxygen species that I can't handle it if I'm on perfect health, right? I need antioxidants because I'm not in perfect health. I'm making too many reactive oxygen species. Can we go back a layer, stop making too many reactive oxygen species, make just enough that I keep the cell perfectly happy, get rid of the bad, be able to recycle the bad mitochondria, have normal autophagy. That's going to be the key.

Dave:

So well said, and thank you. Betsy, thanks for sharing your clinical experience with Spermidine on Bulletproof Radio. I am super excited. It's only been in the country for a little while. The site is Spermidinelife.us/dave, and use code dave25, save 25%. Is there anything you'd like to say to listeners that we haven't talked about, about Spermidine?

Betsy:

No, you guys, I think we've posted some more information on it, on boulderlongevity.com. We have the Human Optimization Academy there where you can go learn. I want you guys, again, I'm preaching to the choir because your listeners are all gigged out on this stuff, but this is where we have to start. The drug companies have learned you've got to talk to the consumer, not the doctors.

We're learning, people like you, we've got to spread this information to the consumer, to you guys. You've got to take control of your health because you can't rely on your doctor to do it. They don't understand this stuff. They don't remember it. You've got to learn that you've got to understand it, and then you've got to take control. If you follow me on Instagram @dryurth@boulderlongevity, and then go to Human Optimization site, which in on boulderlongevity.com.

We have some videos up there that will help you understand some of this metabolic health. I gave a great talk on cancer that's up there, and mitochondria health and cancer that's really interesting because it all comes down to exactly the same source. It really does.

Dave:

Beautiful.

Betsy:

I'm going to join your January 21st group fast.

Dave:

Oh awesome. Thank you. Thanks for mentioning that. Guys, if you go to fastthisway.com, just order the book now. Send me your receipt on fastthisway.com, and we're doing a two-week fast training, or fasting challenge, where we take you through all the different types of fasts, including what's called a spiritual fast. I appreciate that you're going to be there, along with everyone else, and I'm going to suggest that people who are doing the fast, you might want to do it with Spermidine. I will be. Have a beautiful day.

Betsy:

Thank you. You too. Stay well. Bye.

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