

Announcer: Bulletproof Radio, a state of high performance.

Dave: You're listening to Bulletproof Radio with Dave Asprey. Today's cool fact of the day is about hummingbirds. It turns out that amongst all the animals with a backbone in the animal kingdom, the one with the very highest metabolic rate is the hummingbird. When they're hovering, they're about 10 times the metabolic rate of what a human can do on a pound for pound basis. Most of their diet, though, comes from sugar things like nectar and they would be considered diabetic if they were humans, but to burn through that sugar so rapidly, they keep their wings fluttering 60 to 80 times a second and they eat so much food so fast [inaudible 00:00:49] they burn it that they eat one and a half to three times their weight in nectar and insects per day.

The ruby throated hummingbirds have a metabolism 100 times that of a big animal like an elephant, which is kind of cool because we're all animals, we all run on mitochondria, but there are some serious differences between how we sense the environment and how we use what we get in the form of food and light and all the other signals to tell our bodies what to do, which is why as you can well imagine, I've been mastering the art of foreshadowing lately, we might have something to do with metabolism in today's episode. That's because today's guest is a guy I referenced heavily in Headstrong, my book on cognitive function and mitochondrial hacking and his name is Dr. Frank Shallenberger.

He's been practicing as a physician for more than four decades in conventional and alternative medicine. He was a western doctor earlier in his career and found he just wanted to know than what happens in a hospital, decided the body was a self healing mechanism and that our lifestyle, our belief systems, bad exercise and toxins, were what was breaking his patients. As you well know, I am very much in alignment with that method. Dr. Shallenberger is one of the guys who's revolutionized the practice of anti aging and preventative medicine since the very early days of those fields.

In his work, the stuff that really transformed my first recovery from molds, toxicity and all this other bad stuff I had going on including obesity and early risk for stroke and heart disease and arthritis and chronic fatigue syndrome and blah blah blah, all the bad stuff, it was his work on ozone. He has a patented method to measure mitochondrial function, metabolism, oxygen utilization and then can do something about it with stuff that most of us haven't heard of. We're going to talk about it and some of this is in his most recent book called Bursting With Energy. He's also written a book on type two diabetes.

Dr. Frank Shallenberger, it's an honor to have you on the show. Your work is seminal in the field, has made a huge difference in changing the industry of functional medicine. Thank you.

Frank: Thank you for having me, Dave. It's a pleasure to be able to talk about these things, of course.

Dave: It kind of makes me sad. We were neighbors for a while. I used to live outside Lake Tahoe in Nevada and you're in Carson City. I was about 10 miles away from you but I

never knew your clinic was there or we would have just gone out for coffee. Since I'm not there anymore, just for people listening, we're talking live from Nevada [inaudible 00:03:29].

All right. You're 40 years into a career as a doctor. What made you decide that you were going to focus on mitochondria before everyone else did?

Frank: It's interesting. In the early 80s I learned about ozone therapy.

Dave: In the early 80s? That's really early.

Frank: Yeah. I was one of the first guys that actually brought it over here to the US. Interestingly enough, it has a history that goes all the way back to the late 1800s in the US. The Florida Medical Association produced a paper in the early 1900s and the Loyola School of Sciences in Chicago produced a paper in, like, 1885 describing ozone therapy. It does go way back. I was one of the first guys that actually brought it back from Germany in the early 80s.

The thing was after a while I just noticed that unlike most any other therapy, whether it's natural or pharmaceutical, usually these other therapies have kind of a limited spectrum of what they do. It didn't take me long to figure out that ozone is good in almost every case you see. It's good for heart problems, it's good for toxicity problems, it's good for low metabolic problems, it's good for stress, it's good for sleep. It's all these things and you ask yourself, "How can one thing be responsible for improving people with so many different things?" You've got to look at the core, what's core, and you don't have to be a genius to figure out I'm giving oxygen, that's what ozone is, so I'm giving oxygen, everybody's getting better. Ergo, the problem probably has something to do with oxygen, specifically how the body's using oxygen.

That's how I got into the whole metabolic thing. I started looking around and saying, "Okay, we've got to start measuring people's metabolism because I'll bet you an nickel that after I give them a course of ozone therapy, their metabolism's gone up." I developed this technique that you referred to on how to measure mitochondria function and indeed that's what happens. You get the ozone and the mitochondrial function improves. At that point I decided that's the Holy Grail. The Holy Grail is to figure out how to optimize mitochondrial function. To do that, you've got to measure it first. You measure it. If it's great already, fine, there's not much you need to do. If it's not, then that keys you in that it's time to do something, make some changes.

Dave: There are two big things I want to talk with you about. One is that other things you can do with mitochondrial function, but let's first zoom in on what ozone therapy is, assuming a lot of listeners have probably heard me mention a thing or two. Let's talk about how it works, how it's administered and the kinds of things that you see clinically and then I'll share some of my own stories because I've been doing this at home for nearly 20 years. That's not necessarily a good idea for people to do it at home, it can be dangerous but hey, I'm a professional bio hacker, I'm married to an MD, it helps.

What is it? Give us the overview.

Frank: Basically for the audience, ozone is molecular O<sub>3</sub> versus the regular form of oxygen which is the kind that is in the air we're breathing right now which is molecular form O<sub>2</sub>, meaning that while regular oxygen contains two oxygen atoms, ozone contains three. That extra oxygen atom makes it a very unstable molecule, such that when we put it in the human body and you can put it in the human body in a lot of different ways. You can expose the blood to it, that's probably the most common way. You can also put it in various body cavities, stomachs, vaginas, bladders, rectums, wherever. You can inject it into joints, you can inject it into backs, you can inject it into soft tissues. You can give it transdermally in the sense of a sauna where the person's in a sauna and then you flood that sauna with gas and it absorbs transdermally.

However way that you get the ozone in the body, the very first thing that it does is instantaneously react with that third oxygen molecule, such that in actuality the ozone's gone very quickly after you put it in the body. Instead what you have is the reactive products which are primarily lipoperoxides or lipids that have been oxidized. The ozone's gone in essence. Now you're left with these pile of lipoperoxides. They work locally, and that's what works all the magic of ozone, is these peroxides. They hang out locally and they do stuff locally so if I just put it in your rectum it'll have some local application there. Your body will also absorb these peroxides and they'll get systemic and they'll go all throughout your body. That's what mediates all the effects.

Dave: Traditionally speaking, peroxides are oxidative free radical species that are supposed to be bad for us. We take antioxidants, et cetera, et cetera. Why are these peroxides good for us?

Frank: That's a great question. We're lead to believe that free radicals are in fact bad. Nothing in our body that our body makes is bad bad.

Dave: Yeah.

Frank: There's always a reason for it and I don't like it when people come up and say, "Oh yeah, such and such is bad." Paracelsus taught us it's not the substance itself that determines whether it's good or bad, it's the dose. Oxidants and even free radicals in the correct dose, in the correct amount, are actually highly beneficial.

Dave: That's what you get from exercise, right? You exercise, you get free radicals, the body adapts, things improve.

Frank: Exactly. Yeah, that's exactly right.

Dave: In my case, I learned how to do ozone therapy from an 88 year old dentist in the Bay Area who's since passed away. He recognized my interest in this and said, "Oh, let me teach you how to do it," and he was using it for dental patients with incredible results and showed me which gear to buy, told me how to do it and I was dealing with serious brain fog back in the day. It turns out I was living in a house with toxic mold. It causes

autoimmune issues and just exhaustion where at the end of the day you're putting one foot in front of the other but it's every ounce of effort you have and you go to sleep and you wake up feeling hungover and it just never ends.

I did rectal ozone therapy. What that means is you get about a liter of ozone gas which smells kind of like after it rains or after an electrical arc. You don't want to breathe this stuff, it's really bad for your lungs, and you, to put it in a just really medical term, you stick it up your ass with a very small catheter. I did that. I'm saying, "This is a little odd but I'm going to try it." Within 30 seconds of doing that, I felt my brain wake up. It normally lasted for a minute or two but I feel like myself again and then it went away and so I said, "I'm done." I did this every night when I wasn't flying somewhere for about 18 months and every day I would get another minute or two of additional brain function time until a lot of the problems I'd had just went away. It's one of those things where if I wreck my metabolism flying around the world or eating something I shouldn't eat or whatever, I do ozone therapy and it comes right back online.

What happened to me, then? Why did it work like that?

Frank: It's hard to say but obviously it opened up something. That rapid a response, it probably just, these peroxides cross the blood brain barrier. Maybe they had some kind of immediate effect. We don't normally see that. Normally you have to do in the order of 10 to 12, maybe 14 treatments before we actually start to see things like that happen. You got to build up these peroxides in other words. I'm not sure why that happened to you.

Dave: It may have been a lack of blood flow to the brain which is something that toxic mold can do. It could have just been a pure oxygen effect but my sleep quality improved. Since then I've used it on my kids, not that way but local skin infections that really would require antibiotics, gone in two treatments. Really stuff that if you were to just talk about this, people would say that's not possible except it's so routine and it costs two cents worth of oxygen in order to do it. It's so big but it's unheard of outside a few alternative medicine things. Why do you think it's just unheard of in the States even though Germany, Cuba, Russia, it's much more common?

Frank: Most problems probably relate to communication. I don't think we've really been communicating really well with this. On the one hand we traditionally communicate to the people that are already interested in alternatives and that limits it. The majority of the population that could care less about alternatives or care less about anti aging, and so we're limiting ourselves. The majority of doctors out there are not interested in alternative stuff.

One of the biggest messages I have to tell people about ozone therapy is that it combines well with everything else. I'm quick to tell a cardiologist or a neurologist or an endocrinologist or an oncologist, hey, add ozone therapy to what you already do. Do not stop doing what you're doing, just add it in there and do it for about 30 days and then talk to me and tell me that you're not getting instantly better results. That's sort of the message we got to get out there, is it's not one or the other, it works great with what you're already doing.

Dave: When I wrote Headstrong with mitochondrial function as the backbone for making your brain work better, people who are listening who have read it and a lot of you have, thank you if you've taken the time to do that, you know that your brain has more mitochondria per cell than other parts of the body. The heart's also very high in those things. If they aren't working well and you do get more mitochondrial activation, you're probably going to feel it in those areas first.

When I look at every degenerative disease, I mean Parkinson's, Alzheimer's, ALS, autism, some of the autoimmune things, diabetes, they all when you wrap enough layers down, they come down to energy metabolism.

Frank: That's right.

Dave: You have something that you've been using clinically for a very long time that goes to the lowest possible common denominator and you make that better, the foundation gets stronger and of course you can then apply whatever other medical interventions but it makes sense just as a scientist that, yeah, those would work better if there's a stronger foundation and the body has enough energy to fold proteins or clean out cells or do whatever it's supposed to do and we know where the energy comes from now.

In terms of the latest and greatest ozone therapy, there's something called 10 pass ozone where a physician will pull some of your blood out, mix it with ozone, re-inject it and do that 10 times which has a pretty darn big effect on the body but it's also one of the more invasive things. You have to use heparin and take some time.

Frank: Yeah.

Dave: If you put that at one end of the spectrum as sort of the big bad amazing ozone spectrum thing you can do, not bad in a negative but just big bad tough, and then on the other end you can put ozone in drinking water and gulp it and get ozone in the stomach which is the easiest thing you could possibly do. Could you walk me through just a few of the details of all the different things between there, the reasons we might want to put ozone in different places and some of the types of benefits or how we would know when to put it where?

Frank: I'm thinking your question might have something to do with dose.

Dave: Dose is part of it but for people who are listening going, "Okay, I know that there's this gas, I think it's a pollutant in the atmosphere but now I know it's a signaling molecule in the body," there's many different ways to put it in the body. Just kind of walk people who don't know any of that stuff just through the places you'd put it and why and then of course the fact that dose matters, just weave that in.

Frank: Okay. Basically I guess you could break it down to two ways. One is there are [inaudible 00:15:56] ways to treat yourself systemically. In other words, everything gets, these peroxides go everywhere. The best way to do that is actually with the blood because you're going straight into the blood. That is, by the way, you take blood out of the body

into a container, glass or a special plastic, inject ozone, which is a gas, into that container. It mixes in with the blood and instantly creates these peroxides so now you've got a bottle full of peroxides. There's no ozone in there anymore, there's just a bunch of peroxides, and you've got white cells also in there that have been affected by these peroxides. You then infuse those white cells and all those peroxides back into the patient and those peroxides go everywhere and mediate what ozone does. That's sort of the best known systemic therapy that there is.

Other ways to do it are, you alluded to, put it in the colon. The thing about when you put it up your rectum is that these peroxides first drain straight to the liver. That's what drains out of there. It's a direct liver treatment. If you think of hepatitis, you're going to think more that way. Now you might combine them too, do the rectal and then do the systemic in, say, a case of hepatitis.

You can put them locally. If you have conditions of the bladder, either a superficial cancer of the bladder or chronic cystitis of the bladder, you can inject it in there and these peroxides will be locally there. Some of them will get absorbed systemically but now you've got more of that local effect.

As you've mentioned, you can ozonate water. You can then drink the water. You can apply the water into your eyes. You can swish the water around in your gums for dental issues. You can inject the water into a vagina for a douche sort of thing for various ailments down there. You can also, Tesla in 1904 was the first guy that created ozonated oil. He created ozonated olive oil and you can take this oil and you can eat it. It's full of peroxides, so you could eat it, you could put it on tissues, put it on your skin. You can inject the oil. We've injected it into bladders, we've injected it into tumors, we've injected it into rectums. Does that kind of get to the question a little bit?

Dave: Yeah. People listening are thinking, "All right, there's a bunch of different ways that you can use this stuff," and we touched on how it turns on mitochondria by giving them these lipids that are oxidized which causes them to wake up and create more of their own endogenous antioxidants and to function better, but it also has a pretty strong antimicrobial effect. Can you walk me through what happens with [inaudible 00:18:54], fungi, viruses, bacteria, cancer, the whole spectrum of things where it might have an impact?

Frank: Yes. There's two aspects to this. One, ozone the gas is a potent antimicrobial, potent against all micros whether they're viruses or mold or bacteria, it doesn't much matter. Meaning that even small amounts, for example they use it to purify water systems. Las Vegas's entire water system is done with ozone and they'll tell you down there that the ozone is something like hundreds of times more effective per gram weight than chlorine is. It's a very powerful anti, in that case you get the ozone gas directly on the problem.

Now peroxides themselves aren't all that antimicrobial. What they do is they interact with the white cells in your body to induce a greater secretion of cytokines. These cytokines are the molecules that cause your immune system to get rid of the microbial infection. Because the reality is if somebody has a compromised immune reaction and they get exposed to a bacteria, they may not be able to knock that bacteria out and

they're going [inaudible 00:20:15] maybe [inaudible 00:20:16] a antibiotic. Whereas somebody else that has a really active immune system won't require the antibiotic, they'll make their own cytokines and they'll deal with it themselves.

Ozone can up regulate all that cytokine thing by, that's what these peroxides do. In that way they come out through the immune system but not directly, so you got a direct action of the ozone gas, then you got an indirect action against microbes through the cytokine effect on white cells from the peroxides.

Dave: That makes a lot of sense. Going back probably 100 plus episodes, I interviewed Robert Rowen who was using ozone therapy in Africa during an Ebola outbreak and having people get rid of Ebola, several cases he wrote up actually, which is a pretty horrible disease. You mentioned earlier hepatitis. What's your take on using ozone for these chronic infections that just grind people down, even Lyme disease. Are you seeing results from using ozone in places where antibiotics just aren't working?

Frank: The problem with antibiotics is you've got to have an immune system to back them up. When you take an antibiotic, whether it's for strep or I don't care what you got, you're not going to kill every crummy germ in that body. You're going to kill most of them and then allow the immune system at that point to come in and take over. You take the antibiotic for 10 days or seven days or whatever the doctor tells you and at the end of that 10 days, don't go thinking that germ is completely eradicated from your body. It's not, it's there but it's been knocked down to the point that your immune system can take over unless it can't.

This is the problem. Let's use Ebola for an example. It kills something like 85% of the people that are infected with it, but interestingly enough it doesn't kill 10%. What's up with that? That such a virulent organism, how come in the 10%, what's the difference between the 10% and the 90%? Clearly it has to do with immune system reactivity which is why if you take the other 90% and give them ozone at the same time they're getting whatever treatments they're getting, they give them supportive treatments like IVs and such, but you do all that and then do the ozone at the same time, the results are infinitely better.

Dave: I have an example of that. After Burning Man a couple of years ago I started to get styes in one of my eyes and these are essentially infected tear ducts probably from some dust exposure. I got rid of the first one and I tried a bunch of different antibiotic eyedrops. It took a very long time to heal. I got another one a few months, it became a chronic thing. The last time it happened, I said, "All right, what can I do about this," and I put low strength ozone gas, about 20 gamma for people listening, and I drilled a hole in the side of my, funny enough, my Burning Man goggles, kept my eyes close because you don't want to put ozone gas on your actual eyeball itself, and just kept my eyes closed, listened to something on headphones for 20 minutes while ozonating the outside of my eyes which sterilizes everything essentially.

You know what happened? The sty reversed. It never happened all the way and it made just a giant difference when cortisol and eyedrops together were taking weeks to deal with this, it was gone in a couple days.

Frank: Did it stop coming back at that point?

Dave: I had one more time where they started coming back and I did the same with it and it went away. What I'm sure I did is I pretty much got rid of whatever microbes had taken residence there where they're simply gone. I'm doing some other stuff. I've had chronic [dry eyes 00:24:05] for years, I think living in a moldy environment and probably LASIK surgery did that. The better taking care of my eyes, my anti aging plan is to live to at least 180 and I realized I probably want to have functioning eyes when I'm 140, otherwise it's going to sort of suck, so I'm taking more care there.

For people listening, that's a weird example where I've never seen topical use of it on eyes but my daughter had an ear that was going to need really big antibiotics. It was three times its normal size after a scratch from our rose bush. We put a funnel of ozone on it and two days later it's back when Neosporin didn't touch it. I feel like everybody listening who realizes, "Wait, this is a potent thing. It's almost free, the gear to do it at home. If you're trained so you don't breathe the stuff and all that, it runs about \$1,500 and the cheap stuff from China runs about \$300. If you go to a doctor who's trained on how to do it like you are, and I think you actually train physicians on how to do this, right?"

Frank: Yeah, yes.

Dave: There's a wealth of chronic things that have been irritating you for years that can be just overnight or at least over a short period of weeks turned on, in my own experience, in a way that nothing else does but it's totally out of the consciousness of so many people. That's why you're on the show because you the most experienced ozone doctor that I'm aware of. How common is it to be able to find an ozone doctor in the typical city now?

Frank: We formed the American Academy of Ozone Therapy about, I think it's eight years ago now, and we had maybe 250, 300 members, I'm not sure, but these are all practitioners of various sorts. There's DOs in there, MDs, naturopaths, nurse practitioners, anybody with a license that can administer these therapies. People can go to the web site and they can see some referrals there. They can probably just Google their area. Unfortunately, what you say is right. For a lot of people, especially if they're in outlying areas they're going to have to travel to find somebody who knows what they're doing.

Dave: What are the risks of buying some random ozone machine online and doing it at home?

Frank: I wrote a book about this called The Ozone Miracle and it's specifically for laypeople. They can get that on Amazon.com and it kinds of walks them right through. This is how you do rectal, this is the problem you can get into, this is what you've got to look out for, this is the dose. It's like a paint by numbers type of book.

Dave: Tell me the name one more time.

Frank: It's called The Ozone Miracle.

Dave: All right. That is a book absolutely worth reading. I was hoping you were going to drop the name because I couldn't remember it. This is the sort of thing you can do and you can do it safely, but I would not recommend to anyone inject ozone without a doctor's [crosstalk 00:26:55].

Frank: Absolutely. That's potentially an issue.

Dave: You can die. Let's be real straightforward.

Frank: Yes, okay. Exactly.

Dave: For people who are maybe not going to get the book and try and do something, if you breathe ozone gas, what happens Dr. Shallenberger?

Frank: If you breathe ozone gas, Dave as you probably know, you won't do it again. That would be one time only because you're going to spend about the next half an hour to two hours coughing your head off depending on how much you got and how reactive your airway is. If you're unfortunate enough to have asthma, it could be really bad. It could throw you into a status asthmaticus. One needs to be very careful about getting big whiffs of ozone or you're going to be coughing your butt off. That, by the way, is vitamin C.

Dave: Oh, interesting, just oral vitamin C?

Frank: Yeah, so if somebody sucks up a bunch of ozone, I get two of these calls a year usually, I'll tell them to take 20 grams of oral vitamin C and it'll calm down in about a half an hour.

Dave: Oh, that's good. What if you do a bunch of vitamin C before ozone therapy?

Frank: Not a good idea.

Dave: Exactly.

Frank: You're going to create, instead of these peroxides you're going to create a dehydroascorbate, which is beneficial but doesn't do the same thing that the peroxides do.

Dave: There are a lot of people who have been practicing anti aging medicine for decades who, especially if they got started during the orthomolecular time, that was an early name for the field, where very high dose vitamin C was in vogue, 20, 30 grams a day. By the way, I've done that for several years when I was recovering from things and it did have some benefits. What's your take on super high dose vitamin C?

Frank: I don't use it nearly as much as I used to for general purposes, but I'm using, and this would be high dose, right, but I'm using very typically 25 grams of C as a chaser on the ozone therapy.

Dave: Oh really?

Frank: Yeah. By the way, I'm not the only guy doing this. There's a couple of very prominent docs in Europe that are doing this and then Tom Levy is onto this and some of the other docs that have been proponents for vitamin C. You know who else is, Dave Hunninghake, I don't know if you know him, but he's out there at the Hugh Riordan clinic and they do specialize in high dose vitamin C.

Dave: Is it Dave or is it Ron Hunninghake?

Frank: Ron.

Dave: Yeah, I've interviewed Ron Hunninghake, yeah. He was a great interview too for people listening.

Frank: He's a [inaudible 00:29:31] guy, super knowledgeable. The deal is you're infusing these peroxides so now you got a bloodstream full of lipoperoxides, then you throw in the vitamin C. Now these lipoperoxides are already doing their thing, so that's established. As you're putting the vitamin C in there over the next hour and a half, the vitamin C's interacting with a lot of these peroxides producing a redox shift in vitamin C. By the way, you do this with glutathione, get the same effect.

The body reads the redoxed potential of vitamin C and glutathione. It reads it. It monitors it because when it sees that redoxed potential go off in one way or the other, it's going to respond to that. The vitamin C and the ozone actually amplify the response that you get from the peroxides. It's quite fascinating.

Dave: We make a dry liposomal capsule of glutathione at Bulletproof and I do take that after I do ozone therapy, usually about an hour afterwards. Any sense on timing when you'd want to do that? Half hour, hour?

Frank: We do the intervenous right after, immediately after, so right after would be fine.

Dave: We do intervenous glutathione at Bulletproof Labs in Santa Monica. That's one of the things I use when I'm recovering from travel and all but we don't do ozone therapy there because we're more of a nutrient IV and testing facility, not a treatment facility. It's in a separate medical clinic that's part of the model. Those things are missing from a lot of this conversation. How do you feel really good after you crossed the country twice in two days on airplanes? I could tell you, there's usually a needle in my arm if I want to be really at the top of my game and certainly there would be ozone if I had it there.

Let's shift gears a bit and let's talk about mitochondria because in your book, you talk about how ozone in addition to it making that extra oxygen molecule, it also creates a free electron that can enter the electron chain transport in the mitochondria. The mitochondria's job is to make electrons for energy and all of a sudden you're tossing in an extra one. How does that work?

Frank: Okay, there's a number, primarily it works by oxidizing NADH. Are you familiar with that ratio, the NAD NADH ratio?

Dave: It's absolutely in Headstrong and people listening though may not have read it or probably don't remember. There's a lot of science in there. Will you walk us through it?

Frank: This ratio is sort of the Holy Grail of being healthy, is to maintain a healthy ratio of this stuff called NAD, which is a niacin derived molecule, and NADH, which is the reduced form of that molecule. NAD is the oxidized form of the molecule and NADH is the reduced form of the molecule. The way this works is in healthy cytoplasm of a really healthy person with operative mitochondrial function, you're going to have an NAD to NADH ratio of 700 to one. It's gigantic, the shift. It's outstanding, amazing. You think of any differential in molecules of seven to one, you know that gradient is just astounding. This is what pushes everything in that cell. Every single thing in that cell is determined by this ratio.

As that ratio goes down, as the NADH accumulates and the NAD goes down, so as the ratio gets from 700 to one maybe to 650 to one to 600 to one, everything in that cell slows down. It's the oxygen transport system, this electron transport system that you're talking about that produces that ratio.

What's happening is when a sick person comes into my office, I can very quickly say, "Oh look, you're sick, you're old, you're feeble, you got problems, ergo you have a defective NAD NADH ratio." I don't have to measure it because I can measure the mitochondria directly and they'll be down and that tells me the ratio is defective and we can improve that ratio by improving the mitochondria. That's kind of in a sense the major job of mitochondria, is to maintain that ratio.

Dave: What takes that ratio off? I know half of people under age 40, thanks to your research of larger populations, half of them have a problem and everyone over age 40, we call it aging, we have issues with this ratio. What's the cause of the ratio getting disturbed?

Frank: Ah, now you're getting down to it. I would say that one of the most insidious causes, and by that one of the most constant causes, is having birthdays.

Dave: Those damn birthdays.

Frank: Yeah, those damn birthdays are going to mess you up. Normally you're pretty good up until around the age of 40. From 40 to about 50 the only people probably that are going to notice the decline are going to be athletes or somebody that has a performance issue. They're going to notice they just can't do what they used to do, but the rest, all the normal human beings aren't going to start to notice it until like after the age of 50, 55-ish. Then the older you get as the mitochondrial function depresses more and more, it's going to get to a point where everything starts to unravel. For some people that could be at the age of 45 by the way.

Dave: It happened to me at 25. I'm not going back, let's put it that way.

Frank: Yeah. The other things that come to play besides having birthdays are infections. Infections can poison the mitochondria. Heavy metals can poison the mitochondria, most notably mercury, but all the heavy metals, that's how they exert their toxicities, by screwing up the electron transport chain.

Dave: Antibiotics?

Frank: The drugs doctors give, a lot of them, potent, statins, a potent mitochondrial suppressant. Steroids, mitochondrial suppressants. A lot of the diabetes drugs, a lot of the cardiac drugs, a lot of these antibiotics as you just pointed out, the newer, newer chain of antibiotics are actually mitochondrial suppressants. They kill the bacteria by disabling their mitochondria, but at the same time they tend to disable our mitochondria too.

Dave: About 15 years ago I went on Metformin which is a common anti diabetes drug, lowers blood sugar, and the reason I went on it is a bunch of studies came out that said it mimics fasting and it's probably an anti aging drug and a lot of my anti aging physician friends still use it. I stopped using it because there was about a 30% suppression in mitochondrial function and my anti aging predominant theory is keep those guys running like they were when you were 18, assuming you were healthy when you were 18, and you're probably going to live longer and you're going to like your life better anyway.

What's your take on it? There's a lot of benefits to Metformin but it's also got that mitochondrial issue. Are you pro or con?

Frank: I'm very pro Metformin but keep in mind that all these drugs that exert mitochondrial toxicity don't do it the same on everybody. The key is get your mitochondria measured. If a patient comes into see me and they're on Metformin or even on a statin, I'll measure their mitochondria. I'll find a lot of the time it's just fine, those drugs don't screw them up. Other times it's not so good in which case then we have to have that talk.

Dave: That makes a lot of sense. Just like different foods work for different people. Some people eat nightshades and feel good and a lot of people eat nightshades and it wrecks their mitochondria, but how are you going to know? You either measure it or you just eat a lot of it and see if you feel like crap the next day.

Frank: On the one hand, Metformin's listed as a mitochondrial suppressant. On the other hand, Metformin is a potent stimulator because of, it's a fasting sort of thing, of AMPK which is a marked stimulant for that NAD NADH ratio. Metformin on the one hand can suppress you, on the other hand it can actually amp you up by having a fasting type of effect.

Dave: You're a fan of it. I keep waffling about whether I ought to try it again.

Frank: You just got to, whenever you're on a drug and sometimes drugs are needed, you can go get your mitochondria measured and see if it's screwing you up. If it is, that's different.

Dave: I've looked at a ton of tests for mitochondria when I was writing Headstrong and even now as I work on my living to 180, and yours I would say is the gold standard but you've got to go into your clinic or some of the other ones. You were talking oxygen mask, I want you to explain how yours works. When I look at all the online tests, it's very hard to tell what the heck is going on in your mitochondria. When I say online tests, I don't mean quizzes. I mean where you send your blood in or some other substance and they look at various ratios or they culture it with hydrogen peroxide. Is there anything even useful from a blood test perspective or muscle biopsy or anything or do you really have to strap on an oxygen mask?

Frank: Yeah, you got to do the VO<sub>2</sub>s. That's the only way you can functionally, because it's just impossible. Those mitochondria are going to change every second. It's impossible, you've got to get overall globally, how is the overall global function going on in the entire body? You just pull some cells out, forget it, you're not getting any picture at all that's going to be valuable.

Dave: It is definitely true. In the last month, a couple of papers came out showing marked changes in the shape of mitochondria based on very short term things happening in the environment so that they'll get long and stretch themselves out where they're making energy very differently or they'll move around in a cell. It's a dynamic system, so let's go with that. You've got to test the whole system. How does your mitochondria test work? What's all the equipment that people strap on and what do you look at?

Frank: It's so incredibly simple, I can't believe nobody thought of this 100 years ago, but it's just a total no brainer which fits right in my world. All it's doing is measuring how much oxygen your body's processing and as you process oxygen through these systems we've been talking about, you produce carbon dioxide. If you're efficient, your mitochondria are efficient, it's less CO<sub>2</sub> for the amount of oxygen going in. You produce less CO<sub>2</sub>. That makes it efficient on mitochondria. As they become inefficient, as you process the oxygen, per molecule of oxygen you produce more CO<sub>2</sub>. By looking at that ratio, it tells me how efficient your mitochondria are working.

Then by looking at the volume of oxygen that you're processing and relating it to your body fat percentage, your weight and your height, in other words your body mass, we can determine if you're processing a lot of oxygen for your body mass or not that much. We learn those two things, how much oxygen can his body possibly process and how efficiently can it process it?

Dave: All right, and so it's literally riding an exercise bike with a mask on that's carefully measuring CO<sub>2</sub> and oxygen. If the goal is to figure out how good is your body at taking a unit of food, which is already in your body in the form of glucose or ketones, plus a unit of oxygen from the air and making energy from it, you're going to know because you breathe out some amount of oxygen you then used, you breathe out some amount of CO<sub>2</sub> and so it's a closed system other than what maybe comes out through your skin, which is nominal

Frank: Exactly.

Dave: Then we know and there's just no arguing with that ratio.

Frank: We do it over and over again. I'll do it on somebody, wait a half hour, do it again, wait a half hour, do it again. I'll do it three days later, I'll do it every three days. We see 5% differentiating every time we do it but mostly it's rock steady, it hangs right in there until you start doing something about it.

Dave: If you give someone a big dose of ozone, do you see a shift before and after?

Frank: Oh yeah. That's another way we can test things. We can do the test on somebody and give them a form of treatment, whatever that amounts to, put them on ketosis for example, come back and retest them and see what the effect was on the mitochondria.

Dave: What does ketosis do to mitochondria in your experience?

Frank: Almost always it'll double the effect within four to five days. It's astounding. Not always. There's a subset of the population, probably around 10% of people, that really don't do this so well. They are more of the high carb types and they want to eat a lot of carbs. If you take the carbs out, they really do not do fat metabolism all that well.

Dave: I don't know how to identify that 10% and I find even then if they're on a diet that's higher in carbs, not sugar but carbs, if I add Brain Octane, the oil we make that converts into ketones a lot more than coconut oil or regular MCTs, they still feel better from having those ketones but in the presence of normal amounts of glucose. They don't well on a zero carb diet where they force their body to make ketones but they still metabolize a little bit of extra ketone that comes in nutritionally and they tend to feel good on that which is a very rough marker for, it's probably mitochondrial but we never really know because I haven't tested it using your stuff.

Frank: You can identify the people that need to be on a high carb diet. You can identify them because what you'll see on a mitochondrial function is, presuming there's nothing else wrong with them, but you'll see a very high level of mitochondrial function and almost no fat metabolism. We can tell whether their, in real time at any point of exercise or exertion I can tell you how much your cells are feeding off fat versus glucose because when your cells are feeding off glucose, more carbon dioxide is produced per oxygen. When it's feeding off fat, less carbon dioxide is produced, so if I look at that ratio over time during various levels of exertion I can tell you, "Okay, right now you're burning 50% glucose, 50% fat. Now you're burning 10% fat, 90% glucose."

What we see in these people that need the carbs is they burn glucose like crazy but they do not burn fat and they're in excellent shape. If you see that combination, that person wants to be the person that has a high complex carb diet. Conversely, if you get a person that has low mitochondrial function and is feeding entirely off sugar, you've got a problem.

Dave: That would have been me when I weighed 300 pounds.

Frank: You went through the ketosis, you come back in five days and your mitochondrial function will be doubled, easy.

Dave: That's my experience over and over with thousands of people. The trick there is Bulletproof Coffee has Brain Octane in it for a reason. People drink it like, "Why do I feel so much better?" There's some mitochondrial science going on there. The other thing, and I want to get your take on this, is a recent study from UC San Diego showed that caffeine, about two small cups of coffee worth, doubled ketone production. Is caffeine or coffee, and these are separate substances, but is either one of them something that's good for mitochondria in your experience?

Frank: I love coffee. The data on coffee's awesome because of all the polyphenols in there, so I love coffee. Now I understand some people can't tolerate it because that's just normal with everything, but this study you're talking about, they're talking specifically about caffeine. If you just got caffeine tablets-

Dave: Yeah, it was caffeine tablets that they used.

Frank: I can understand that because it's going to give you an adrenaline effect and adrenaline is a potent, epinephrine is a potent fat mobilizer.

Dave: It would just increase ketone production through epinephrine. They didn't say the mechanism, they just showed [crosstalk 00:45:50].

Frank: I'm pretty sure that's the mechanism.

Dave: Okay, got it. I definitely know that that combination, which there's all sorts of reasons that I think, synergistic reasons that it works the way it works, but in my own life, turning my brain on, having been a former raw vegan and autoimmune issues and then obese and just recovered from way more than most humans deal with, and then to be at the peak of my health in my mid 40s, I know it's because I managed my mitochondria like crazy, I regularly have ketones in my system, I take mitochondrial stimulators. We manufacture some as supplements, things, unusual delivery systems for PQQ and ketogluconic acid and precursors and d-ribose and all these different things and I rotate them around and all, but the difference in the clarity in my thinking and in my ability to fly across the country and not be a zombie, it feels superhuman to me. I do everything because that's just how I am and that's also because I don't want to go back to where I was.

How much mitochondrial stimulation does the average person need to feel a difference, whether it's ozone or something else?

Frank: How you feel can be misleading. You can have somebody that feels really tired and rundown because their adrenals are no good, this is classic, and in actuality their mitochondria are just fine but they feel like crap. When I went and talked to patients

about that, I said, "Think of those guys that are in the Tour de France. They obviously have pretty good mitochondria but at the end of the day, they're pretty pooped out." That's how it goes. You can have great mitochondria and you'll still have your adrenals wasted.

The other part of it, if your adrenals are really good and your mitochondria shot, you might actually say to yourself, "I feel pretty good." Now what you won't know is how do you feel when you ride your bike up a mountain pass because people that say, "I feel really good," and at the same time have poor mitochondrial function are basically people that sit on their butt all day long and they never really test it out. They don't know what their maximum might, they're at such a low level of existence they don't really notice the difference.

Dave: Okay.

Frank: Athletes notice. Regular people don't necessarily notice that their mitochondria are going bad every year.

Dave: The first place it shows up in my research is cognitive function, those little tweaks on cognitive function because you have so much mitochondrial density in the brain and, "I can't quite remember that," more than emotional crankiness. For those people, you give them a mitochondrial stimulant whether it's ozone or any of these other compounds, their emotional regularity improves to the point that the stuff we use in Keto Prime in two different studies is now approved for claims on, "improves the emotional symptoms of PMS." You get that additional crankiness that comes in, you take something that, I'm hypothesizing here, the mechanism action is that it's increasing mitochondrial function because it does it, and then all of a sudden people have better emotional control. Do you see that in patients that report improvements in mood when you work on their mitochondria?

Frank: Interestingly enough, when you're talking I'm thinking about a psychiatrist in New York that reported to our society a couple years ago that he finds that ozone therapy is pretty good for all kinds of these mental disturbances that he sees. I thought that's pretty darn interesting, what's the mechanism behind all that?

Dave: It's probably half infectious and half mitochondrial.

Frank: That brain needs, it figures a lot of stuff out. You want it to be working pretty well.

Dave: You do indeed and that's one of those things, as we look at an aging population, that's one of the first things that goes and a third to a half of people listening, if they don't do any of this stuff that we're talking about, if you just play the odds, they're not going to know their name at the end of their life, which is really sad. I don't think it's necessary anymore. What's your take on Alzheimer's? What are the big things in your 40 years of clinical practice that are probably preventative?

Frank: Oh boy, that's right in there for it. I do think it's a mitochondrial disease for sure. We do know that at least in culture, if you take brain cells in culture and you put various chemicals on them you can induce beta amyloid plaque in those cells. We do know that as we all get older, that beta amyloid plaque's going to be higher in you when you're 70 than it was when you were 35. Now presumably we'll keep it down to a minimal amount so you got to be really, really old before it affects you, but Alzheimer's in my world is not really treatable. We're just kind of getting to stem cells. Maybe with stem cells, but outside of that it's not been treatable, but it's entirely preventable. It's one of those disease I don't think anybody really has to get.

Dave: Dale Bredesen's work lately has been really seminal. I just interviewed him here with The End of Alzheimer's and there's some profound, hopeful stuff even for people who have early onset Alzheimer's where I think you can stave it off for a long time. I would not be opposed to those people starting out with a little bit of ozone along with the other lifestyle changes.

Frank: Yeah.

Dave: Now you've been practicing anti aging medicine, you're a member of the American Academy of Anti Aging Medicine. How long do you think someone who's 20 years old today can live if they're managing things right?

Frank: Let me put it to you this way. The best way to live long is don't get sick. Don't get a disease. That's what's knocking people off. The listeners can just ask themselves, "When's the last time I heard of somebody dying of nothing in their sleep?" It reminds me of an old Redd Foxx joke and he used to ask, he used to say, "Imagine all those health nuts," he'd be smoking a cigarette and drinking whiskey while he was saying this, "Imagine all those health nuts laying in hospitals dying of nothing." That's the deal. If you just don't die from these diseases, if you prevent the dang diseases, and that's all mitochondrial, you do not get sick if you have healthy mitochondrial. I never see anybody sick that's got good mitochondria and I never see anybody who's healthy and vibrant that doesn't have good mitochondria. It's just that's the way it taps out.

Now the thing I like to get though is early on the mitochondria start going south for a good 10, 15 years before a disease actually shows up. You [inaudible 00:52:40] wait 'til you get that, you want to check your mitochondria early on. If it's great, fine, but check it once a year because at some point something might happen. You don't know what that's going to be, something might happen and your function, it happened to me. My mitochondria function was awesome until about 63, 64 and then it just went to heck. There were a number of reasons for that but had I not been checking it, I would not have known that. I felt fine, so to speak.

Dave: Were you able to fix it?

Frank: Oh yeah, I was able to fix it. The reality was I was eating crappy, I was drinking too much, I was stressing out, I wasn't on my regular exercise deal and I was having birthdays. When you add it all up, just so you can switch it around but my point is that's

the point of action where we ideally want to take is early on before something happens. Because whatever happens to me and however long I might live, I want to die sort of naturally, whatever that is. I don't want to have a disease.

Dave: How long do you think you'll live?

Frank: Gosh, who knows? It's a really fascinating question, but I'm hoping I make it to 100. I don't care how long I live, I just want to be able to ride my bike up the mountain passes. That's all I care about. I want to be functional. I do notice that I can ride up the mountain passes at 72 years old now very nicely, not at the same time I did 20 years ago but still pretty good. I can ride around Lake Tahoe which is what, an 80 mile ride with 4,500 feet of elevation, I can do that any old day that I want. Not as fast as I used to but I mean I look forward to having that functionality as I get older. At least to 100. I hope I can get to 100 and at least be functional like that.

Dave: You're already so far ahead of the curve. There aren't a lot of people in their 70s who can do that and I greatly admire the first generation of anti aging medicine founders who are living the, "Physician, heal thyself," sort of thing. The fact that you can do those things says that you might know a thing or two about this and that you have the wisdom to apply your own stuff to yourself. You look vibrant and healthy and your system works and you're measuring that it works and taking people whose systems don't work even if they're 30 and then turning them back on so that they can have 70s like you are, which is fundamental to anti aging.

Frank: One of the things I have always been so interested, I've been in this anti aging movement for a long time but you know what got me into it is I'm just egocentric. I want to know how I can live long and never get sick because as a physician that's been doing this for getting up to 50 years pretty soon, all day long you see people come in who are in one way or another miserable from a disease or a condition that's totally preventable. I don't want to be that person, so I really come from my personal perspective on this. That's why I'm so passionate about it to a large extent, is just for me. I don't want to get sick. I want to live a long time.

Dave: It's okay to be selfish from that perspective. When you have all that energy, it lets you treat your patients, it lets you be with family, everyone around you benefits too, but yeah, no one wants that. Just to admit, "I don't want that, I'm not going there," is actually a little bit of an act of courage so I'm happy you've chosen to do it because your work has definitely had an impact on my knowledge for things. I've one more question for you though.

Frank: Okay.

Dave: Dr. Shallenberger, if someone came to you tomorrow and said, "I want to perform better at everything I do as a human being," based on everything you know, everything you've lived, what are the three most important pieces of advice you'd have for me? What would you tell them?

Frank: I don't know if I could boil it down to three but I would say at the top of the heap, the single most important thing is being in great cardiovascular condition, not acceptable cardio, be an athletic type of, almost up there, just great cardiovascular condition because that's where most people go south, is in the cardiovascular system. That's just huge. By the way, we used all that VO2 data that we were talking about to establish that program for people because that data could tell me exactly where they need to be.

After that, I'm thinking hormones. Especially in hormones, thyroid, especially thyroid.

Dave: Which controls mitochondria, of course.

Frank: I lean on that because the thyroid blood tests that are typically used are just not reliable and we can determine whether somebody needs thyroid or not based upon their metabolism and actually could get to the correct dose that way.

Those two things come to mind immediately. Diet is clearly in there. Probably the biggest, hugest problem with diet is carbohydrates for the majority of the population, so that's pretty huge. I don't think you can actually pick on one thing but if I had to I'd pick on exercise.

Dave: You didn't say anything about happiness, meditation, relaxation, stress. Is that part of your thinking or is it something that's maybe number four on the list? I'm just kind of curious. You have so much experience in this stuff, I want to learn. What's your take on all that stuff?

Frank: Over the years, I have a quite a few patients that just come in here every year and I check their mitochondria. They could be in their 50s, 60s, whatever, and normally they're fine, everything's just fine, but I could tell you all kinds of interesting cases where they come in for their annual, their mitochondria are in the tank and literally the only thing that has changed in their life is stress. They exercise the same way, the hormones are good, the whole nutrition, the diet, everything, nothing's changed except they've been very stressed out. Somebody in their family is sick, they're going through a divorce, they've got bad lifestyles where they're running in jets all over the country or whatever. Things have changed from a stress perspective and those mitochondria, the literature's pretty clear, you can screw them up pretty much within a matter of minutes if you get all stressed out.

Dave: That's definitely something you pay attention to.

Frank: Yeah.

Dave: Do you meditate regularly? Do you do something like that?

Frank: I pray a lot but I'm not really into meditating that way, like blanking out the mind a little bit. I might do it a little bit in the morning sometimes but that's not a big part of my particular program.

Dave: Got it. Well, prayer is in that bucket of, there's many different forms of meditation, but you spend some time thinking about something else. Very cool. You've got a lot of information on your site. It's [antiagingmedicine.com](http://antiagingmedicine.com). You've got that URL clearly because you've been in the business for almost 50 years now. Back when they invented URLs, you were there.

Frank: Exactly.

Dave: I want to say thank you for your seminal work there on mitochondria and on ozone therapy in particular and just helping to spread awareness of that because everyone listening to this show today can probably benefit right now from ozone therapy and there will be a time in your life where you might be looking at buckets of antibiotics or ozone therapy, you might want to hit the ozone first and use the antibiotics second if you need them still.

Frank: Absolutely.

Dave: All right. On that note, thanks again. Thanks for being a guest on Bulletproof Radio. We really appreciate your work.

Frank: Okay, thanks for having me, Dave. I enjoyed it very much. Take care.