



**Transcript of “Doug McGuff: Myokines, & the
Endocrine Nature of Muscles - #164”**

Bulletproof Radio podcast #164



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Dave Asprey: Hey, it's Dave Asprey with Bulletproof Radio. Today's cool fact of the day is that humans have evolved to have larger skulls and we like to think anyways smarter brains. It seems like a pretty good idea except for the way that your skull makes room for your larger brain is by using less bone here in your jaw. What that means is it's harder for us to eat tough food which is fine because that's where we have rib eye. On top of that, our teeth will stay the same size even though our jaws are smaller and that's one of the reasons that you can get impacted wisdom teeth just because your brain's too big. You could also say is because your mom or your grandmother ate grains which can also cause impaction of your teeth.

Today's guest has been on the show quite a while back and it's my great pleasure to introduce a guy who I really consider a ground breaking exercise guy. This is Dr. Doug McGuff. He's an ER doctor. He's an exercise geek and a weight lifter. He's one of those few ER doctors who happens to have his own gym called Ultimate Exercise.

He's one of the authors of Body by Science along with John Little looking at what high intensity training does for you. I've used his techniques for a very long time to support my own lifestyle which is minimal amounts of exercise for maximum gain.

Doug does an amazing job of helping people to understand what they're doing from an exercise perspective. It's been more than a hundred episodes back when Doug was on. We've met him in person a couple of times. Doug, I'm just stoked to have you back on the show.

Doug McGuff: Awesome, I'm really glad to be here. Hey, my wisdom teeth, they came in no problem. I think my brain must be too small.

- Dave Asprey: That's too funny. Don't have wisdom teeth problems because you're dumb, that's really the headline.
- Doug McGuff: I've had to study more than most people that you know, oh well.
- Dave Asprey: You're just something right because you've come up with some new stuff. The reason that I wanted to catch up with you aside just to get an update because I know you're constantly researching this stuff but even looking at Mayo kinds.
- Doug McGuff: Yeah. That's my new obsession these days. I certainly didn't come up with it. I stumbled across some of the research about it and there were always these things that I just believed but could not prove. The Mayo kind is starting to fill in a little bit of that black box for me.
- Dave Asprey: What the heck is a Mayo kind? I'm sure everyone driving right now is just wondering, what is this?
- Doug McGuff: Yeah, Mayo kind is basically just a chemical signaler. The more generalized term for that kind of molecule is called a Sito kind. There are all kinds of Sito kinds that do chemical signaling endocrine signaling from one organ to another or paracrine signaling within a single organ to direct the body as to what it should be doing at any given moment.
- They've recently discovered that skeletal muscle is not just this really great tissue that contracts, makes us strong and able to move but it's actually one of our largest endocrinal organs in our body and it signals to other tissues in our body in a very meaningful way.
- Art Duvetyne a long time ago made mention of this concept that the tissues in your body don't necessarily all just work together in this harmonious passion necessarily. In a lot of ways, body tissues compete with each other and a lot of this competition takes place through Sito kinds specifically, body fat and muscle tissue have Sito kinds.

This signaling hormones that work in opposition and in competition with each other and how you eat and how you exercise can give the competitive advantage to one side or the other such that reaching optimal health. Optimal body composition even optimal neurological functioning can be augmented by tipping the balance in favor of one versus the other.

Dave Asprey: What are some of the most famous Mayo kinds? I know a lot of Sito kinds. I monitor inflammation in a lot of the bio hacks in the [Bulletproof diet book](#) are around oh look, you can lower this specific inflammatory thing with this nutritional intervention or sleeper's stress but Mayo kinds are sub-category of Sito kinds correct?

Doug McGuff: Correct and most of the Mayo kinds that have been studied are actually Sito kinds that have an anti-inflammatory effect and much of the Mayo kinds will have an anti-inflammatory effect that directly opposes the inflammatory effects.

A lot of the inflammatory Sito kinds probably the longest known and most deeply understood Mayo kind is one called Interleukin 6 and that Mayo kind is liberated from contracting skeletal muscle particularly when it's doing high intensity work but pretty much in any sort of muscular activity.

It is released to some degree and it is actually as the intensity of exercise rises, it's released in exponentially greater degree because it is done by an amplification cascade. Meaning that when it's triggered two molecules will trigger four molecules and four molecules will trigger eight and it just amplifies very quickly.

Dave Asprey: That's a beautiful bio hack because what you're saying then is by modifying the intensity of your exercise your basically exponentially increasing the amount of an anti-inflammatory substance in the body?

Doug McGuff: Correct.

Dave Asprey: Wow.

Doug McGuff: It has the sea in time inflammatory effect but it also has neat biochemical effects. It very aggressively up regulates the uptake of glucose into the muscle cell and glucose utilization and glycogen mobilization. It also ramps up lipolysis.

Mobilization of fatty acids from stored body fat and it's ramping through the cell, through the mitochondria to do beta oxidation of fatty acids all of that is augmented and ramped up by Interleukin 6. Other things that it does, is it stimulates the release of nitric oxide which causes basil dilation.

Increase blood flow into the skeletal muscle but has the more long term effect with modulating blood pressure towards more optimal levels and it actually access a leptin surrogate to increase insulin sensitivity so it has just this one Mayo kind has so many beneficial effects that we're looking for.

That's the thing that I always intrinsically felt about high intensity strength training is that it was so much greater than some of its parts. There seemed to be something more going on in terms of body composition then could be accounted for simply by the energy that it used.

Dave Asprey: You mean exercise isn't just to burn calories?

Doug McGuff: Yeah, no.

Dave Asprey: This is fascinating because nitric oxide has been really identified as a signaling molecule in the body that we didn't know that much about even, we'd just five years ago as a major signaler. It just sort of popped up.

Doug McGuff: Yeah, let's see. Interleukin 6, it's probably known about in some research done on it for the past 10 years but the interest in it has gone up exponentially and the neat thing for me as an exercise geek is I started doing this stuff back in the 70's.

I've always been an exercise geek over the long span of time and what I've noticed is that all the major advancements and exercise

physiology don't come out of exercise physiology. They come out of cell biology and bio chemistry.

Dave Asprey: Amen, yes.

Doug McGuff: Freaking geeks that have never exercised in their whole life. When they find something that's relevant to exercise, then you really got something. There's very little that comes out of exercise physiology literature but really has an effect or changes anything at all but when it comes from some bio-chem geek, man, you're onto something big.

Dave Asprey: Everything that you just said, probably like I'd say in my experience I'm not certain that it applies to muscles although I think it's pretty darn likely in my experience but you focus on that more. All of the brain training and cognitive stuff that I worked on, the same exact statement about when you change something at the cellular level.

Everything above it including the way you think and your ability to pay attention, all of that changes so I'm going to send you. I think in September 10th I'll have my early things, a new mitochondrial thing and we're calling the whole body neutral paid called [unfair advantage](#).

It's the single most exciting new supplement I've done as important to my own performance now is [Bulletproof coffee](#) that up-regulates your mitochondria and just basically you can feel within five minutes of taking it in a big way.

I'm predicting that would be like new world record set from people using the stuff because just like you said, what happens when you fix something at the cell level, it just goes throughout the body so I honestly have never been more excited. We'll ask and give you this stuff. It's not even available for pre-re yet but when it comes out, everyone is going to talk about it.

Doug McGuff: That's cool and here's another thing about this Interleukin 6 is it is an anti-inflammatory molecule but it's not just the effect of the

molecule. It's the effect of its receptors so it's not only anti-inflammatory. It's pro inflammatory in terms of its receptors.

If you're generating lots of Interleukin 6, then you up regulate Interleukin 6 receptors sensitivity and when that happens, it has that pro inflammatory effect of ... Actually, I'm saying it backwards. More Interleukin 6, you down-regulate the receptors. The fewer receptors you have, the less inflammation you generate.

Dave Asprey: Wow.

Doug McGuff: That is the molecule anti-inflammatory, the down regulation of its receptors is anti-inflammatory so it's kind of a double whammy with the production of this Site kinds.

Dave Asprey: I'm inherently a lazy guy who calls strategic laziness, where like I'm not lazy because I don't want to do the work. I just want to do the work faster so I can do something else that's more important. Can I just get a IL-6 nasal spray or inject the stuff down rigor in my receptors and just not even pick up something heavy?

Doug McGuff: You know I'm betting that there are pharmaceutical companies working on that right now. Now, there are genetic manipulations that can be done to increase or decrease your production and a lot of the research that's been done on how Interleukin 6 is based on taking it away from experimental analyst. The way they do that is bio genetic manipulation that produces an Interleukin 6 knock out gene so that you basically, you know?

Dave Asprey: Wow.

Doug McGuff: The DNA is just a big series of bases, cytosine added to it and guanine and it's this little code and if you just brain shift the code a little bit, whatever transcribes with that particular gene will now become garbled nonsense and then the animal doesn't have Interleukin 6 anymore.

Then in an animal devoider severely hampered in the production of that harmonizing and figure out exactly what it's doing.

Dave Asprey: Wow. What about that bacteria? Do they make IO6? Is there is a gut biome component to this whole thing?

Doug McGuff: That I don't know and that's my other big fascination that I'm way behind the curve on is the whole intestinal microbiome and I'm certain that it has some sort of interaction but I've not really tweezed that out of anything that I've read so far. Like I said, I'm just kind of scratching the surface of this stuff but it's pretty cool stuff.

Dave Asprey: It's remarkable how many of the different Sito kinds are in some way manufactured by the gut bacteria to the point that in the research that I've been working on the bold pure diet book. Like these little bastards, some of them are good for you but a lot of them are they're hacking your system.

Your body has its own regulatory system for inflammation and then these little things sit in there and they said, oh we wanted you to be more inflamed or less inflamed for our own nefarious uses which is mostly keeping their life support system alive.

I'm intrigued to see what happens when they look at both high intensity exercise plus gut biome and is there some group of people who work out really hard but have a bad gut biome and either it doesn't work because that was my experience.

An hour and a half a day of heavy lifting for half of it and heavy cardio for the other half, I couldn't lose weight granted I was over training like crazy but I weigh 300 pounds and I was desperate and I'm certain in retrospect, in my gut biome was the part of the whole equation but you know ...

Doug McGuff: Yeah. I think that's probably going to turn out to be true and it will probably true in a feed forward kind of way in the sense that if you're doing proper training and it's high intensity at its brief enough and should be able to recover from it.

If all these people have trouble with recovery or you're just totally hammered for two days after work out, I'm highly suspicious that the answer might be that somehow your gut microbiome is disrupted but in the feed forward mechanism, I think the delivery of an appropriate exercises stimulus may release those Mayo kinds.

In such a way that drives behavior towards re-establishing a better gut flora so I think that both can benefit the other and both can harm the other depending on what you're doing. I think if you're someone that's going to chronically over train.

That clearly gut inflammation from ischemia related over training marathon runners can really disrupt you gut microbiome and in that process, turn you into someone that's just a poor exerciser and poor recover.

Dave Asprey: Yeah. My little memory trickle bookmark was accurate. I just pulled it up. There's this study from actually 10 years ago where they were looking at the effect of MCT's. The stuff in [Brain Octane](#) and the [MCT](#), that when you combine that with a bacterial toxin analogy of bad bacteria in the gut.

That only in that case in rats that [MCT](#) changes these secretions of Interleukin 6, the primary Mayo kind we're talking about. There's an interesting thing from what you eat based on the toxins made by what's growing in your gut.

It changes your inflammatory profile basically how you respond to it. It's so complex and it's so amazing that what you're talking about which is will just down regulate your receptors by lifting heavy things sometimes. It seems like an elegant way to get around a lot of these complexities.

Even if you have a problem with your gut bacteria, you're still getting less of this problem.

Doug McGuff: Yeah, the more I read on this that's the cool thing about all these complexity is all of that complexity and all of these feedback loops seem to benefit us by making what we have to do very simple.

All of that complexity and all that adaptability means that we just have to have a few gross heuristics to operate within in order to optimize everything and all the complexity of that will take care of it for us.

Dave Asprey: Doug, that's one of the things I really like about your perspective. You dig in way more than most people would because you're an exercise geek and because you have a little bit of training that went into your medical degree and so you have this way of thinking.

This body of knowledge and you've gone in with that level on exercise which lets you make those basic heuristics like one of the questions I'm sure people have got to be asking themselves. You've talked about the benefits of lifting heavy things.

To basically down regulate your IO to upper glade to production heuristics and down regulate the number of receptors you have so you'll have less inflammation but how often do you have to do it?

Doug McGuff: That depends upon the individual and the recovery status at any point in time but the more we lay, if someone is interested in optimizing their results really don't have to do it that often and overtime, I really like working out and I will do it as much as I can get away with.

Even though I'm a huge advocate of appropriate recovery and doing very brief workouts and frequently so to answer your question, I think it is always in exercise a great idea to strive for a minimal effective dose because exercise is pro inflammatory.

Dave Asprey: Okay.

Doug McGuff: If you are a person that is not living life right, not eating right, burning both ends of the candle all the time, you have to

understand that the exercise that you're doing at least in the acute phase is adding an acute inflammatory event onto a chronic inflammatory state.

When you're making this transition from let's say you're finally going to say look, I'm going to take care of myself. I'm going to live life right. It's most important for that person to do exercise in a way that invokes the pro-inflammatory state but does it in a way that allows you to make that transition without chronically heaping more and more stress and inflammation onto a chronically stressed and inflamed body.

Minimal effective dose is a great way to do that. As a 52 year old guy who has no major injuries from training over the longer term, it's also important because really what you start to find out is, you experiment with all of these different ways of training is that all the extra crap that I did through the years didn't make a difference.

That actually the best results came when I truncated and minimized my training and really paid attention to recovery and diet. Things on the recovery side of the equation.

Dave Asprey: Yeah.

Doug McGuff: You can get the hammer and pound the shit out of the nail but if you really tune the recovery side of the equation, you don't have to hammer and hammer and hammer. The training becomes a nail gun not a hammer, you know?

Dave Asprey: What a beautiful analogy and I wish someone had told me that when I was 20 at the gym, six, seven days a week and it was exactly what you were describing. I didn't understand that you should recover like a demon not exercise like a demon.

Doug McGuff: I don't know if the younger guy will ever listen to that. I mean so much of having to be tough in your youth just has to do with the fact that you're just fucking stupid and you just need to be tough

because you're stupid until you get to have accumulated enough who wants to actually become smart.

Dave Asprey: You know what, I've got a five year old boy and a seven year old girl and I've got to say and maybe it's just the fact he's a boy, I mean it's going to hurt if you do that and then he looks at you and then he does it anyway. I'm like well, it's a learning experience and we've got iodine for that or whatever it is but it's funny because it continues.

We know the pre frontal cortex really finishes and solidifies around 24, somewhere around 23 and 24. During that time, there's a whole set of these behaviors that are sub-conscious that come out and I beat the crap out of my body.

I have a screw on my knee and three knee surgeries before I was old enough to have my pre final cortex all the way in because I wouldn't listen to my body and I also was doing things that was supposed to be good for me that just simply weren't.

That's one of my motivations for what I do now is let go. Like why don't we do what just works because I was strategically lazy when I was under 23 and I finally have to do what I want to do it but I just thought I had to do things that were actually bad for me.

That's kind of an obnoxious thing and you're saying though that you like to exercise so you work out as much as you can get away with. Now, I get clients like that when I do coaching and with the [Bulletproof Diet Book](#) coming out is getting to be harder and harder to do one on one coaching but I still make some time for this.

There are often times like type A career CEO's, celebrity type so they're working really, really hard so not enough sleep, frequent travel, they also want to be Ironman athletes. They want to do some seriously intense stuff and then you look at their blood pulse.

They're clearly the CRP is high, their HRV, the higher variability is all not right so classical over training so then you tell them, look you need to back off a bit and then they look like they're going to cry and say but I need my exercise.

It makes me feel good and there's some OP addiction there but there's a comfortable line between having to beat yourself up every single day. Where do you draw that line if people want to exercise more than the minimum effective dose? How do you know if it's too much?

Doug McGuff: The way I tell people to assess it themselves is if something comes up in your day to day life on a day when you're scheduled the workout and if something interferes with that and you have to cancel it and move it to another day.

If it freaks you out or if it pisses you off or if it ruins your day and you're in a foul mood the rest of the day or you can't stop thinking about it, you're doing too much. That is the weird thing about the over training syndrome is, it is a form of OCD.

It's like telling someone with OCD stop flicking the lights switch man. It's not good for you. Well yeah but if they don't, they're going to feel enormous angst over it and that angst is the signal that you're there and this is why I like your concept of strategic laziness because that's what we evolved out of.

We want the most results with the least efforts because in the evolutionary environment from which our body's evolved out of that was an absolute necessity because there was really severe scarcity. Now, in the age of the modern age where capitalism does provide and sell independence, we've got a mismatch of that.

Yeah, I find that amongst hard driving executive types that you service is this whole Johnny Quest mentality that I'm going to work 16 hours a day, I'm going to travel all over the world and I am going to run marathons, do alter endurance and events and climb mountains.

All these Johnny Quest crap but in the end, once you end up figuring out is that in order to be superhuman, you have to realize that you're only human and when you have accounted for that and followed the biologic imperative to cover and take care of yourself with the appropriate nutrition and the correctly modulated exercise.

It's then and only then that you really do feel superhuman. I think that's a big, big key in all of these and it's a hard thing to get these hard driving individuals to understand.

Dave Asprey: It's really something I didn't understand but resilience is itself a practice and no one's like, "Good job Dave" you're really resilient. You're strong and you didn't give up and bottom line is giving up is one thing. Deciding that you've had enough and that you need to recover now so that you can get up again the next day and do it over is just a different scale.

It's not one that we praise. It's not one that we train and it's not one that really you're likely to know about unless you've hit the wall really, really hard a few times.

Doug McGuff: Yeah, I just was watching a video clip and an interesting thing is you talk about a Navy SEAL or Special Forces type people. Those people are put under huge amount of stress both as a weeding out process but also as stress inoculation to make them.

Dave Asprey: Yes.

Doug McGuff: But what they found is in all of their stress inoculation training, the one thing that decreased the washout rate at buds from 38 down to 23% was one simple thing and that was to teach combat breathing which is a meditative form of breathing.

Where if you're freaking out and you need to slow your heart rate down because once your heart rate goes above about a 140 fine motor control and decision making capacity is a bunch of crap and what they do is they taught these guys how to meditate and how to breathe. Four seconds in, hold four seconds, four seconds out.

Dave Asprey: The box breath.

Doug McGuff: Yes, the box breath training and learning how to meditate that alone proved more valuable in terms of stress inoculation and making it through the buds course than all the other more traditional stress inoculation techniques that they had done.

Stress inoculation is a good thing and it's good to challenge ourselves and do big things but again, that whole realizing that you're only human to become superhuman is important. There are elements of self-care that make you able to handle those stressful moments.

As an emergency physician, it's taken me, I've had a 25 career in this including residency so 22 not but along career and emergency medicine and it's going from a new ER doc to an old ER doc, one thing I've really come to realize is that the answer to dealing with this uncontrolled pace.

Overwhelming pace and in sick people and dying people is not to get yourself all amped up on Redbulls and all hyped up and crazy. You got to have an ability to calm yourself to be the eye of the storm in order to function truly well.

Now you can get yourself through it when you're not as good as you should be by drinking Redbulls and going ape crazy but the better way is to have that kind of calm.

Dave Asprey: It's funny you mentioned the medical side of things. I've learned those meditative breathing techniques in all the 40 years as a neuro feedback and all that sort of stuff so I've learned to calm myself even at in an ER which you saw it's been always terrifying.

I made a commitment to training my kids the same way so both my kids play the hard math game. The inter balance sensor that you clip a little thing on and just last night, Ana who's running and she tripped on a stair and landed skin to all four joints you can scan at one time.

Screamed and it was a disaster and she sat up and literally did four full slow in, slow out breathes, stopped crying, picked herself out and decided she wanted to go into the forest before we cleaned up her wounds.

I was just flabbergasted to see this because just teaching those basic skills, I mean what would happen in the ER if everyone who came in with whatever kind of critical injury they have knew how to breathe like that? Do you think more people would survive? I don't want to put you on the spot. I know you have license and issues or whatever but ...

Doug McGuff: Well yeah, I know you're talking about this surviving. I kind of suspect that it might be because one thing that we found is that in critical care patients, someone that is a bad multi trauma or someone with bad sepsis that you have to put on the ventilator.

That if you don't provide appropriate pain control and anxiolysis, that their mortality is actually significantly higher. If you have a big dumping of catecholamines during an acute injury or illness, your survival is actually worse.

We try to manage that pharmacologically and through medical intervention but now that you asked the questions, someone that was able to access their own physiology like in my opinion every human being should be taught to do.

Dave Asprey: Yes.

Doug McGuff: If they were able to do that, I think it could make a real difference.

Dave Asprey: Probably not in some cases.

Doug McGuff: People that are under acute stress, their ability to manage their own physiology can save their life in a critical situation but certainly I think it could also diminish the likelihood of developing PTSD during a stressful event or something.

Because all of these big dump of catecholamines and inflammatory cytokines I think has a long term effect for setting the stage for those sort of bad things. I've not thought this out, I had a time before you're asking me but when you ask me that I think yeah.

Dave Asprey: You know what you're doing because according to my friends over at the heart math institute, I'm an adviser for [heart math](#) and just a friend and supporter of their kind of technology.

They've looked at that and people who are trained in heart rate variability before they go into combat are less likely to get PTSD because they can get out of fight or flight so it's funny that you predicted that based on your knowledge from ER. That's startling that you did.

Doug McGuff: Funny that you asked me that because now when I think back about it, right now I work the past 20 years I've worked in a high volume, high acuity community emergency department but when I was in residency and we rotated amongst different big hospital at the children's hospital.

They had a specialist called a child life specialist and per my recollection when the children were in painful or stressful situations they would come in and they would actually talk them through breathing exercises and things for self-calming.

It really did make a significant difference so I think we do this for a kid, why don't we do this for everyone and for adults. That's probably something that could be applied in the emergency medicine setting that would be beneficial for a lot of people.

I tell you, I get the sense that on any given shift on any given day, 40% of what I see is driven largely by anxiety states.

Dave Asprey: Now here's an odd question and then we'll go back to some of the other exercise related stuff. Could you set a ventilator to do box breathing?

Doug McGuff: Yeah you can.

Dave Asprey: Does it calm people down?

Doug McGuff: I don't know.

Dave Asprey: I'm so intrigued.

Doug McGuff: You can set a ventilator mostly what we manipulate ventilator settings for is to do three things. One is to control the level of carbon dioxide that's circulating the blood by how well you're blowing off carbon dioxide and to what extent.

The other is to affect oxygenation of the blood and third is to provide pressure support for when the lung is ill, when it's got fluid that's causing the oval line to collapse and things of that nature. Mostly the ventilator is tweaked to optimize acid based balance in the blood and to optimize cardiac output. To answer your question, some critical care specialist that's very adept at ... you could.

Dave Asprey: Wow, I'm so intrigued.

Doug McGuff: What we're finding with ventilator settings is it used to, 10 years ago, we would run much higher tidal volumes and respiratory rates than we do nowadays. Now the tidal volume has gone down significantly and the level of oxygenation and respiratory rates have been modulated somewhat. Some sort of sense that would be the ventilator version of that kind of approach.

Dave Asprey: Let's take on back to exercise. Given that you know so much about blood gas mixes more than anyone with a degree in exercise physiology is likely to, have you applied that to exercising and oxygen tends high altitude velocity of training, lifting heavy things without any error, stuff like that?+

Doug McGuff: No, not really. Other than the thing with breathing and exercise is the same thing that we're talking about earlier with the complexity of my kinds and get back to all the stuff. If you're doing

really hard work, the best ventilator mechanism that you can use is the one that you don't think about. It auto regulates very well.

When you're doing hard, high intensity exercise, you start to generate a lactic acidosis from the production of lactic acid. The automatic response is that PH is received by the chemo receptors in your arteries and around your brain stem.

Automatically regulates the respiratory volume and rate to blow off carbon dioxide to affect carboxylic acid in your blood stream to normalize the PH relative to the lactic acid doses. That kind of auto regulates. Go ahead, it looks like you're going to ask ...

Dave Asprey: No, there's a whole school of training, mostly for endurance guys around live high, train low or vice versa depending on stuff. I've been for the past almost month or so getting my blood oxygen levels very short intermittent phases down into the high 70's for up to six minutes at a time.

I'm in the middle of basically trying to raise my EPO levels naturally for as an anti-aging technique. I've noticed huge differences in how I feel after just a few days of that and it's shown to improve athletic performance but it's fascinating to look at high intensity exposures to really heavy exercise which you just figured out with some of the latest research you're doing.

What is doing on my own kinds and the number of my kinds. It appears you can do the same thing with cold, the same thing with blood gas levels. There's all sorts of ways like reach into the body and give it a strong signal to make it change even though that's a signal that might never have really occurred for most people in a normal way of living. I'm intrigued that we're going to find a lot more there.

Doug McGuff: Yeah, oxygen is a whole different model than carbon dioxide monitoring for the body because how oxygen is moved around the body is through hemoglobin which is a really cool molecule, it's a tetramer.

It has four binding sites per oxygen. It changes its chemical shape as it binds oxygen. If you have a tetramer with four binding sites and you bind one oxygen, the remaining three binding sites attract oxygen more aggressively.

Then you bind the second one, the third one and the fourth one now bind more aggressively when they're all four bound, hemoglobin holds on to oxygen very aggressively. A lot of people think of optimizing their oxygenation means having better oxygen binding.

That's not the case, what you need is oxygen delivery, the hemoglobin molecule has to be able to let go of oxygen at the tissue level. At sea level when you chronically have good high levels of oxygen, you're always binding oxygen aggressively and it's hard for the oxygen to let go at the tissue level.

Things that can augment letting go of oxygen at the tissue level acutely are lactic acidosis and signals that there's tissue hypoxia. That changes again the shape of the hemoglobin molecules so let's go of oxygen more readily.

On a chronic basis, when you train at altitude or you do what you're doing, you're actually up regulating a molecule called 23 Diphosphoglycerate and that as a molecule that changes the shape of hemoglobin over the longer timespan so it binds oxygen less aggressively.

Dave Asprey: Really?

Doug McGuff: That means you're able to let go of oxygen more easily at the tissue level. What you'll find is if you train at altitude, you return to a more normal sea level, what you'll find is that your oxygen saturation rather than always being 99 or 100%, you'll be at 95%.

Someone that's trained in a hypoxic environment produces more 23 Diphosphoglycerate and they therefore bind oxygen to the hemoglobin molecule a little bit less aggressively and are therefore more able to let go of oxygen at the tissue level and pass

oxygen from hemoglobin to myoglobin within the muscle where it can be utilized.

Dave Asprey: You're increasing the bio availability of oxygen to your muscles?

Doug McGuff: Correct, by actually holding onto it less stingily.

Dave Asprey: Doug I'm so glad I asked you that because no one's ever explained that to me. I don't even know that molecules and I have to go look it up.

Doug McGuff: The cool thing is, can you see me on the screen?

Dave Asprey: Yeah. Although people who are in their cars won't but a lot of people in YouTube or iTunes ...

Doug McGuff: I'll try to describe it verbally. The oxygen binding curve for hemoglobin is Sigmoidal. It starts of very flat and then as oxygen level rises in your blood stream, when the partial pressure of oxygen is about 20.

Your oxygen saturation is going to be 50, 60% There's a partial pressure of oxygen rises to 30, 40 and 50, you get on the steep part of the curve that goes up too. Once you get a partial pressure of oxygen about 70 or 80.

Your hemoglobin molecule will be about 95% saturated and then you can drive oxygen up to partial pressure of 200 and you're not going to get ... you're still going to just bottom out at 99 or 100%.

The shoulder where you go from really tightly bound oxygen and fully saturated hemoglobin, is at about 95%. Someone that's trained in a hypoxic environment will sit right at that shoulder.

If they can drop off under the steep part of the dissociation curve really quickly. That person lets go of oxygen more aggressively at the tissue level. A lot of people when they do this and they put the pulse axe and like damn, I'm only 95% on there.

This isn't working. What that really means is that it is working, you should be running around 95, 96% not a hundred percent. Think I'm getting worse when they're actually getting better because your binding oxygen less aggressively so you can deliver it to tissue more easily.

Dave Asprey: Serendipity is awesome because I put on my pulse oxygen monitor and it was just at 96 and I was like god damn, literally it happened to me 30 seconds ago. Yeah, I've been monitoring my blood oxygen, I wrote about what happens to it when I fly.

I've been playing with this for years and then I guess all the stuff I'm doing, first time I saw 96 during the day and here it is you predicted that.

Doug McGuff: More is better. When it comes to hemoglobin binding, you want to bind the oxygen less aggressively. Most people that are well conditioned will float around 95, 96% because they let go of it easier.

Dave Asprey: That's beautiful. Let's get back into exercise. Cross fit and functional movement, what's your take on ... the intensity is there and it seems like minimum effect of dose isn't going to give you the benefits of proper form that you would get from a functional movement training.

What's your take on that from body by science perspective?

Doug McGuff: I don't ever want to be a guy that comes across as a hater and in that context, I go to the cross fit website every day and I look at it and I like their sense of life.

Dave Asprey: Amen, yeah.

Doug McGuff: I think there is enormous value in doing hard things. I think that's cool stuff. The whole functional movement craze is a little off-putting to me because I think it's overplayed.

The human body if it's appropriately strengthening and conditioned is functional and can get into most positions pretty well. I don't think you have to construct a major training component dedicated exclusively to that for that to be in place.

My beef with cross fit from the body by science perspective is two things. One is that for most circumstances and most people, you have crossed the threshold way beyond minimal effective does.

If you follow the wads and you do what's going to be going on at most boxes, you're going to be well beyond minimal effective does. What that does for cross fit from the marketing standpoint.

It creates the fitness version of seal buds training. You kind of get rid of all the people that are not intrinsically tough enough to handle it or don't have that genetically gifted recovery capability to begin with.

You kind of weed out the weak and you're left with the strong. It's a great marketing strategy for getting people that respond well to exercise. It's certainly greatly oversteps the minimal effective dose concept which I'm a big fan of.

The second thing is I think they need to rethink a lot of the different wads that are named after women, I don't even know what they are but I think it can be a real problem when you take a highly complex skilled movement pattern and mix it with exhaustion.

Because motor skills like we said before, motor control degrades when heart rate elevates above a certain point, complex motor skills degrade with exhaustion. When you're going to put a 500 or 2000 meter row and a hundred per piece before you do some complex Olympic lift.

I think that's the prescription to mess yourself up in a big way.

Dave Asprey: You worry about the injury side of it?

- Doug McGuff: Yeah. Not in body by science, super slow, a lot of the high can see world, we are way on the other spectrum of safety. We invoke so much safety that our margin of safety is almost ridiculous. Ultimate exercise has been opened since 1997, we do 120 workouts a week, we've never had an injury in facility.
- Dave Asprey: Where is your facility? Plug in for a minute.
- Doug McGuff: We're in Seneca, South Carolina which is right next to Clemson University if anyone's familiar. We have this huge barge in safety. I'm not saying that everything that they do is unsafe but I think there are certain combinations where you're begging for it.
- If you're really doing something that's highly exhaustive, that's stacking a lot of fatigue and a lot of lactic acidosis and you're going to do a complex motor movement in a state of exhaustion. That's when you're going to drop the bar on your neck or on your back or you're going to lose control whether going overhead and Terry rotate the calf, would get a slack injury.
- I think some of that probably needs to be rethought or people that are doing it well are probably arranging things in a way where that doesn't happen.
- Dave Asprey: The composition of the wad really matters for cross bed. I hear you there.
- Doug McGuff: That's their product and that's their business, I'll let them handle, I got my product in my business.
- Dave Asprey: I don't think neither of us is dumping ...
- Doug McGuff: I love anyone that values doing hard things, I think it's cool.
- Dave Asprey: I even have a Kelly Star as it comes to the bullet proof conference to speak and he's doing some of both. I'm a supporter of it but man if you're going to train that hard, you better recover just as hard and a lot of the techniques that I've worked on are good for recovering resilience.

Whatever kind of the stress is and if you're working out six days a week, your physical stress is pretty high. Let's hope your emotional and job stress aren't so bad.

Doug McGuff: It's the way they market themselves with all the military devotion and all the workouts named after bed soldier. The whole Johnny quest Special Forces things really appeals to the type A executives that you've spoken about earlier.

That can really just throw gasoline on the fire of the OCD over accomplishment leading to over training problem that we talked about earlier.

Dave Asprey: It's something that I think is here to stay that's super high intensity and it feels good and the community. There's a lot of good stuff going. I hear what you're saying there, the concern about injuries because me, I'm actually grateful that I walk relatively normally because after my third knee surgery at 23 where they put a screw in my knee.

They sort of said well, be grateful you're walking and for me to have gone from constant knee pain in both knees to being able to trek at the Himalayas for months even though my knees hurt some of the time to be honest. It doesn't matter, I could do it and it was within my capability and I didn't have an unstable knee or anything.

Doug McGuff: That's a cool point that I've noticed over the years both in the emergency department seeing patients and in the training. I see a lot of people with bummed up joints, bad knees osteoarthritis but the people that are doing high intensity muscular work can have a knee that by radio graphic criteria is horrendous osteoarthritis. They're asymptomatic, they don't have pain.

Dave Asprey: Wow.

Doug McGuff: Whereas someone that is not doing exercise that challenges muscle in a meaningful way, those people have osteoarthritis with

inflammatory changes and significant pain that limits their activities of daily life.

I think it has a lot to do with this mild kind stuff we've been talking about. One of them in a Luke in 15 has a big systemic anti-inflammatory effect mainly by the fact that it antagonizes trampled body fat which the major distributor of all these inflammatory sitachimes.

It also has a direct anti-inflammatory effect as it circulates through the body and that's one of those things that I observed but could not explain that I think miochimes might explain and it might explain why you got this knee that's full of hardware. Does that really bother you that much when if you looked out on X-ray, anyone in the right mind will do?

Dave Asprey: Shit. That may be the case because I did not know you were supposed to be able to walk without pain until sometime in my mid 20's. I actually did, I played soccer for 13 years, it hurts to run, it hurts to move, that's just the condition of life.

I had extreme inflammation because I was exposed to some bio toxins and whatnot. I ate like crap because we didn't know any better. Mistakes were made but still, looking at all this isle six, isle 15, isle 8 like all the different in a loop then.

All the Miochines are ... it's been revolutionary for me and you've studied them much more than I have, I've looked at which supplements and in some cases which forms of things like cold thermogenesis are going to regulate inflammation because unlike aging as a war against inflammation so how do we win? Are you going to come out with a book on these? It seems like it's about time.

Doug McGuff: Man, that would be cool to do, the next go around, I'd like to do another exercise but it incorporates all of these stuff again. I probably will have to do that, it's not definitely in the plans right now because there's just so much other crap going on right now.

Yeah, especially as my understanding of it, delve deeper but the cool thing about it, it's kind of the cool stuff about what you do is that all of these complexity and all the stuff that you can really geek out on.

The neat message behind it all is that if you just follow some simple heuristics in, just do this, then all of that takes care of itself that complexity is there to make it simple for us.

Dave Asprey: It's funny, I did not know half the reasons [Bulletproof coffee](#) works. I experimented with this idea of putting butter as better than other crap that's in cappuccino and because I felt really good, I just noticed that into bed.

As I wrote the bullet proof diet book, I kept coming across research and my god, someone actually did this study and they found the same results that I kind of noticed it myself but I didn't know there was any science behind that. I was able to kind of geek out and find reasons that I was getting effects that should not have happened according to my expectations but did.

Doug McGuff: Yeah, that's the thing over the years, experimenting in the gym that and reading and communicating with other people that are experimenting. I started to see the pattern because everyone thinks that science always precedes invention and innovation but it doesn't.

Invention and innovation precedes science and then we give science something to fill all these science that's coming out on high intensity exercise was preceded by 20 years by guys like Arthur Jones and Ellington Darden and people that were looking into high intensity exercise and just intrinsic intuitive.

Man, this is really good stuff. That preceded any scientific investigation into why it worked. What I'm really starting to understand is that there's something that precedes innovation.

It's called tinkering and farting around. This farting around and tinkering with shit leads to innovation and then one the

innovation expresses itself, this side is like hey, what are these guys doing over here, let's study it.. That's the way it goes, science never precedes innovation that I have ever seen.

Dave Asprey: Looking at observation, a little bit of hypothesizing and experimenting and then you really come in with the hardcore stuff. I just funded some research looking at inflammation and I just paid for the IRB approval for a study and it's funny, it's an observation that I've made that I'd say thousands of other people have reported to me but no one's ever studied it in a systematic way.

Okay, either the inflammation numbers are going to go up or go down according to a set of practices and that sort of thing. There's no real economic incentive for much of this ... who's going to benefit from doing the study on high intensity exercise, some new gym or something maybe? It's not like it's a big pharmaceutical company. I'm really looking forward to more quantified self-happening.

Doug McGuff: I have this book that is called body by science and I have been dogged by people for a lack of scientific rigor and some of the stuff I discussed on the internet on my blog and in videos and with you and you've got a lot of crap.

Guys like us what we're doing is we throw dog shit at the screen door and see what lands on the other side. When some stuff lands on the other side then the serious scientist come pick that stuff up and run with it.

Really, that willingness to kind of say this works for reasons I don't understand and I'm going to keep doing it even though I can't prove it is enormously beneficial and sometimes the proving it part of it, that doesn't happen for 20 years. You don't have time to wait around.

Dave Asprey: Aging doesn't wait and I'm not planning on dying because I was waiting for double blind study that said dying was bad for me.

- Doug McGuff: I'm 52. Tomorrow I go to take my board every 10 years you got to recertify for your board certification emergency medicine. Tomorrow I go take my second 10 year certification which means the last time I took it I was 42 and I literally feel like it was two weeks ago that I drove down to the testing center and did it.
- Dave Asprey: Wow.
- Doug McGuff: The thing is in our day to day lives, the days are long but the years are short. We all don't have time to mess around with this stuff. I believe this got to get on with it and do things.
- Dave Asprey: It's totally true and I got to say, if you're watching and you're looking on Skype, you don't look any older than I am and I'm 41 so you're doing something right. I look odd today if anyone's noticed me sitting with my eyes closed.
- One of my eyes is fully dilated because I had an eye exam right before this. I've been kind of like squinting and looking funny the whole time.
- Doug McGuff: Look like Satan.
- Dave Asprey: I've got two more questions for you. One of them is have you looked at inflammation or muscles and whole body vibration at all, it seems like there's another whole set of hacked warm up kind of stuff going on there. Full disclosure I have no bullet proof vibe, it's a very small part of what I do.
- Doug McGuff: This is the second time someone's really ping me with that. I had an interview with Joseph Mercola a while back and he pinged me about it. It triggered me just enough to kind of hit pub Ned and see if there's any literature out here about that at all. There seem to be a mother lode of it but I have not delved into it yet.
- Dave Asprey: You want me to send you one for three months to play with? I'd be happy to.
- Doug McGuff: Sure yeah.

Dave Asprey: It's yours. The bullet proof vibe is awesome. I stand on it like probably between this and my next interview, I'll go stand on it for 2 minutes just to get the lymphatic system going, circulation and all.

Doug McGuff: To answer your question, in any real sense, enable to be able to comment intelligently on it, no.

Dave Asprey: Okay cool.

Doug McGuff: It did peak my curiosity enough just to go let's look and see what the lyrics are like. There's a lot. You got to be red.

Dave Asprey: It goes back to that whole kind of strategic laziness, minimum effective dose and I'm a big believer in movement and one of the things I love about your book body by science.

Look, taking this to Aris's movement, it's not exercise. You're not getting a hormonal response. Sometimes I don't have time to go for a walk but I still want my body to get... the movement that happens so if I can accelerate that into a smaller period of time. Maybe inferior but it's better than nothing.

I tend to look at it like that.

Doug McGuff: It's not exercise but I think that kind of stuff is important because one thing I'm also becoming a big believer in and my own kind is kind of feed into that. The concept of signaling.

I've always found that when I spend a lot of time walking, long distances, hour or two walks, go on long walks with the wife, I'm always leaner. Not only of any exercise affect or calorie burning effect but I think it's in the biological signal that says look.

If you're going to be moving around that much, the diminishing marginal utility of carrying stored energy on your body is too high. Its cost is too high. Sure you got two weeks of stored energy but the cost of carrying around all that crap is too much if you're going to be moving around that much.

The biological signal adjust behavior in a way that allows you to be leaner, it's not that you're burning calories or 10,000 steps a day burns a certain number of calories, that's crap.

Dave Asprey: It's laughable.

Doug McGuff: I do think it sends a biological signal that says the marginal utility of having stored body fat is now diminished.

Dave Asprey: I think we would both agree that there's got to be something going on there. Same thing, it doesn't make any sense because you burn three potato chips worth on your long walk if you're really looking at calorie burn.

Yeah, you feel better and I always assumed it was something to do with the muscles effect on them for you to increase lymph flow and maybe you have more ability to burn fat. There's clearly some mechanism that we ...

Doug McGuff: Yeah, things are so much going on inside that black box that we just got to be happy what comes out the other side.

Dave Asprey: The other question I really wanted to ask you is something that I think would benefit readers. Bullet proof exec is relatively complex, there's a bunch of come here, start here kind of stuff but really, there are people who get into the weeds and there's a lot of weeds there that you can get in to it if you want to really go do something.

When I go to bodybyscience.net, you've got a lot of complexity on there too and I want to know how are you dealing with that and where should new people want to go and check out your website, where should they go to start looking at your recommendations because honestly you've got tons of stuff on research.

I find it as useful resource.

Doug McGuff: That's a great place for ... it's more of a gathering community for geeks like me that want to come there and geek out. I actually

have a website that I run most of my consultancy through that has a direct link to a YouTube channel that's got some good videos and lectures and things of that nature.

That's just drmcguff.com. If you go there, you can see all the stuff on consultancy but there's links on learn and watch and stuff like that where you can go and pick up some of the lectures that I have given that have been recorded that really kind of part it down into the essentials. It can even be much simpler than that and it's ... you have a great visual analog thing for diet that I think is just a great heuristic to operate by.

Dave Asprey: Thank you.

Doug McGuff: My heuristic for diet is this. For exercises, do something really hard every once in a while and remain active otherwise.

Dave Asprey: That's too hard, let me write that down.

Doug McGuff: Do some really hard stuff, every once in a while and remain active. Diet is this. If you draw a straight line between the sun and your body then that's a good diet. It can be ... your diet can be you getting directly in the sun and converting vitamin D3 and probably a lot other hormonally active substances that about that come from direct sunlight. Or the sunlight acts on phytoplankton and the sunlight acts on plants that go through photosynthesis, you can eat those; Terry Wahl's eggs.

Dave Asprey: Yup, she's a good friend.

Doug McGuff: Or, there are animals that eat those plants and you can eat those animals and you can move up the food chain. That food chain is a chain that connects between you and the sun in a straight line. When you deviate off that straight line through processing, that's where you get into trouble.

A diet that stays on that straight line tends to be a single ingredient diet. You don't pick up a box and it's got 40 ingredients

that you can't pronounce, you pickup ... what am I going to eat, I'm going to eat an egg, what's an egg? Egg.

What's an apple? Apple. What's in broccoli? Broccoli. Single ingredient diet, straight line between you and the sun and that works out but the heuristic, that little analog thing, good, better, best for each of the different macro nutrients and stuff.

That's a great gross heuristic and I think those are the things, those gross heuristics that simplify everything so that you can do it without having to devote so much mental energy to it. You can go on and do the more important things in life. I think that's really key.

Dave Asprey: I think we have a similar way of thinking because I think you really wrote it down in your book, same thing when I read them. I don't need to know all the details here. I'm more about feeling really good having a ton of energy, having my brain work all the time.

Looking reasonably, I'm married, I have kids, I don't have to have a chiseled Hollywood 6% body fat. In fact, I would probably die sooner if I did like most people who went that way.

The whole point there is the goals are different but when it comes to exercise I know you've gone two levels deeper than I have and I look at your ... here's the five things you do and do them about the soft and grab this little intensity. About there. You're not too perfectionist about it, love it, that's perfect.

Doug McGuff: Yeah. There's a letter of the law and I love digging into that. The purpose of letter of law is so that you can operate with the spirit of the law. If you do that, you're 95% of the way there and the rest is just icing. If you just want to geek out, it's there for you.

Dave Asprey: It's time to test your memory because 100 and so episodes ago, I asked you this question, I don't want to ask it to you, it's the final question in the interview. What are your top three recommendations for people who want to perform better at life?

If you want to kick more ass, do these three things. It doesn't have to be anything to do with exercise, whatever else but you've learned a lot, you have an interesting career. The three things that everyone should know and we're going to test and see if this matches with what you did before. Not really, there's no test.

Doug McGuff: It won't match because I've seen your other interviews and I saw the question and I thought, what do I want to say this time? It's probably going to be different than what I said before.

Dave Asprey: That's actually good.

Doug McGuff: It's not going to relate just directly to exercise or physical aspects but life in general, because I'm studying for my emergency medicine boards third time around. This time the renewal every 10 years, it gets me thinking about things in a more global sense. In the global sense, my three things for kicking ass in life are number one.

Just show up, just show up. That's 90% of it. Whatever it is, just do it, just show up and be there and you're on your way. The number two thing is imagine.

Actually if there's something you want to do, somewhere you want to be, being able to imagine it in your mind sets the stage for it to happen. You give your brain and your mind a target to focus on and that starts with imagination.

Then once you've done that, the other thing is rehearsal. Just rehearse it in your mind over and over again, there are certain big things that you have to have worked out in your mind ahead of time.

You know what your course of action's going to be because when the shit hits the fan and you're freaking out, you got to be able to go there. When I go to work in the ER every day when I'm driving into work, I rehearse three things in my head. One is to do a thoracotomy which is where someone's been shot in the chest, they arrive in full arrest, you got to open up their chest, open up

the sack around the heart, evacuate the clot. Save someone's life, that's been shot or stabbed.

The other is the procedure of a Cricothyrotomy which is getting into the windpipe for someone who has had massive facial trauma or is having allergic reaction or tongue so swollen that you can't get a tube into their windpipe by the usual route.

You have to do it surgically. The third is a post mortem cesarean section. A pregnant woman that's beyond 20, 24 weeks gestation that's had a cardiac arrest would then find a cardiac arrest, the only way you're going to save the mother and the baby is to cut and get the baby out.

The thing about emergency medicine and the thing about so many things in life is the greater your need to act quickly and decisively, the greater your tendency to hesitate.

The only way to overcome that is rehearsal. Think about the big important issues in your life and how you're going to behave when those things happen and rehearse them every day.

When it does happen, you'll know what to do. When you're on the 114 floor of the world trade center and the instruction, they told us just to stay put until they give us instructions.

If you thought it out ahead of time, you'll be the guy that says screw that, I'm going down the stairs. When someone holds you at gunpoint in the parking lot of the shopping center and says get in the car, you'll be the guy that says I'm not getting in the car.

You can shoot me right here in the parking lot in front of all the cameras. There's all sorts of things, you got to pick what they are. Whatever these big issues in your life that you foresee coming sometime in the future, think about what you're going to do and rehearse it. Those are my three secrets to kick ass.

- Dave Asprey: Those are definitely more impactful than the last ones because I'm not sure I remember them without going back to look at the show but I think I'll remember these Doug.
- Doug McGuff: Ravidly scrambling here on my computer trying to find the old episodes.
- Dave Asprey: I would have been said if you said the same ones because people can always listen to the first interview. By the way you should if you enjoyed this one, the first interview was going to be talked a lot more the basics of exercise and all.
- Doug McGuff: Doug it's always a pleasure having you on the show, would you toss out DrDougMcGuff.com and .net. Any other URL's besides those that people should go to?
- Doug McGuff: I think that will get you to everything that is sort of a portal. Drmcguff.com and bodybyscience.net and you can find me from there.
- Dave Asprey: Wonderful, have an awesome afternoon and thanks again for being on bullet proof radio.
- Doug McGuff: Yeah, send me a copy of that book. I want to see it.
- Dave Asprey: It's coming.
- Doug McGuff: All right boss.
- Dave Asprey: You've probably heard me talking about whole body vibration on one podcast or another but if you haven't, check out the bullet proof whole body vibration platform called [the bullet proof vibe](#) on [upgradedself.com](#).

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