Danny Lennon: So onto today's episode I'm going to be joined by Dr. Mike T. Nelson who has a PhD. in exercise physiology from the University of Minnesota with that work specifically focused on the concept of metabolic flexibility. Previous to that Mike did a Masters in biomechanics and currently he's an adjunct professor and a member of the American College of Sports Medicine, as well as working with a ton of private clients online on both training and nutrition and like I said for a long time Mike has been really deep in the weeds on this area of metabolic flexibility. In fact, me and Mike first did a podcast episode way back maybe the start of 2014 so what four and a half years ago around this concept and really I wanted to get a kind of updated revised view on some of these ideas and to ask some deeper questions about this concept and to really get rid of some of the misconceptions that still lie around what metabolic flexibility is and what influences that.

So hopefully this is an extremely informative episode. We're going to get into some definitions. We're going to talk about some of the ways metabolic flexibility relates to performance and then we're going to turn and look at how metabolic flexibility plays a role in overall health as well as the progression of many chronic diseases and metabolic diseases as well. So lots of interesting stuff here. I'm going to link up to anything we mention in this episode as well as a transcript over on the show notes page which is sigmanutrition.com/episode250 so as ever that's the way you can access any episode that you listen to the show sigmanutrition.com/episode and then just fill in whatever number episode you wish and you'll get to

the show notes page. So for this one that's /episode250. So let's get into this week's show with Dr. Mike T. Nelson.

Mike welcome back to the podcast and what I think is your third appearance on the show so hat trick of episodes with you. So how have you been doing my friend?

Mike T Nelson: I'm in new and great. Yeah thank you very much for having me back on here again for the third time. Really appreciate it.

Danny Lennon: Yeah we've had some really good conversations in the past and there's definitely some things I want to hear your views on now and there's plenty to get into and discuss but just before we do maybe as a way to catch people up to speed if maybe they haven't caught you on previous episodes or are unaware of your background can you bring us through some of the overview basics of the work you've done, your area of expertise within your academic career and PhD. and so on and some of the cliff-notes that they should know about you and your work.

Mike T Nelson: Yeah so the brief version I did a Bachelor of Arts Natural Science and then I did two years postgraduate work in mechanical engineering and then did masters actually in mechanical engineering, biomechanics got done with that. So I was never going back to school, did five years in a PhD. program in biomedical engineering dropped out of that and to go over and do exercise physiology which my PhD. took seven years. So I don't recommend that much college to anybody and was looking at heart rate variability and metabolic flexibility. The formal title was fine scale variability across physiologic systems. So we're using some math to try to get at heart rate variability and then also to look at possible non-invasive way of measuring metabolic flexibility. So I've been working with clients for almost 12 years now officially. So I count that as the time I'm actually charged money and not the probably 8 to 10 here so spent writing free programs and doing all sorts of horrible stuff now that I want to head slap myself for doing but you know everyone starts somewhere. Yeah and then right now I'm a faculty member at the Carrick Institute. They do functional neurology and I help them design a course on human performance with Dr. Kenneth J. Dr. Freddie Garcia and some other guys there which is by the time people here this will be out which is awesome and I'm also teach online for Rocky Mountain University, Georgia Southern University and then I work with clients online both kind of continuing the program and one-off sessions and then I have a certification which is the Flex diet. It's flexdiet.com. It's kind of a mash-up between metabolic flexibility and flexible dieting. What I wanted was just a framework where I could take

all the interventions for kind of training more on the I guess we should say nutrition recovery side and put them together in a framework that coaches and clients can then learn and then also make it applicable as soon as possible also.

Danny Lennon: Awesome and I think that's definitely going to play into much of our discussion today and I remember going all the way back to your first appearance on the podcast which I guess was maybe over four years ago now at this point we discussed metabolic flexibility quite a bit and I want to get into more of that today because I think there's some things that have popped up over time that particularly now with a lot of things that are of interest to people I think with even if they don't realize it may be directly relate to metabolic flexibility and I also have seen some may be miss-interpretations of what that means or maybe some misunderstanding of the role it plays. So maybe to frame all this and to get everyone up to speed how should we define metabolic flexibility or at least how do you get that concept across the people so that we could really kind of grasp what we're talking about when we use that term.

Mike T Nelson: Yeah how I explain it is there's all this disagreement about what is the best fuel to use in training and the reality is if we simplify it down to the two main fuels which are fats and carbohydrates both of them are to me the best fuels to be used it just depends on what you're doing. It's a metabolic flexibility if you look at a spectrum on the right end we have carbohydrates, on the left and we have fat. Metabolic flexibility would say okay how well can your body use carbohydrates how well can your body use fat and then how well can you switch back and forth between both of those fuel sources. So it's kind of three parts right carbohydrate use, fat use, and then the ability to switch back and forth between those. So it's the ability to use the right fuel at the right time. So it's kind of respecting the context and then also the dynamic nature of physiology.

Danny Lennon: Right and I think that's the kind of key thing of seeing that we have these different fuels that we can use and there's benefits to using them at in different proportions at different times but also a key component will probably come back to later as you discuss is the ability to switch between them and the speed at which someone can do that. One area that I think probably as you've seen a lot of the misconception maybe stems from is when people are trying to do either a training or nutritional intervention that someone has told them increases fat burning and typically this is when if we're looking at say a respiratory quotient for example getting them closer to the say 0.7 or in like you said on that scale moving them to

proportioning using more fat than carbohydrate to be oxidized and just when we use that term fat burning I think for a lot of people can be misleading and thinking that well anything that generates more fat oxidation is inherently better. Can you maybe touch on the kind of –are these potential flaws in that thinking and what may be a more accurate view of thinking how we can influence our fuel use with training and nutrition?

Mike T Nelson: Yeah. So the first part the big question there is do I want to use more fat as a fuel depends on what I'm doing and we'll get into maybe a little bit more high-level athletics after this but I would say in general if I'm at rest or doing a lower intensity work I want to be able to use fat as the main fuel. The big benefit of fat is indirectly can help with body composition, we will calories aside for right now and then you just don't really need to be running anaerobic metabolism at rest. If you are man you're going to be in a world of hurt. So using fat anaerobically so using an oxygen at rest or low intensity activity is going to be beneficial. The catch for people kind of get all mixed up is when you start throwing performance in. So I would say performance on the right end of the spectrum is probably going to be much more carbohydrate, ATP-CP that type of fuel system.

So I think up regulating the use of fat as a fuel is a good thing as long as you're expecting to use it under the right context and conditions which by definition is more on the lower intensity spectrum and again all these things are just like it's not an on and off switch is more like a dimmer switch. So we're just kind of trying to push you to use more of a percentage of it from fat and in terms of how people do that for your listeners you probably already know this but it's generally lipolysis which is how do you liberate fat and get it into these smaller little chunks into the bloodstream and then fatty acid oxidation or "fat burning" so how well do you actually burn fat as a fuel then. And if you look at most of the literature it's really – it's pretty clear that lipolysis really isn't limiting meaning that your body will liberate more fat than it will use and it's the fatty acid burning or oxidation of that fuel that's more of the rate limiting step.

So from there you can make an argument that on recovery days on easier days my bias is that most of that work should be done in a fasted or semi-fasted condition. I actually want insulin levels to be a little bit lower. So insulin is more of a fuel selector switch which I stole from Jeff Bullock [ph] so when the insulin is lower it pushes a body to use more fat as a fuel, the insulin is higher pushes the body to use more carbohydrates. Now

again it's not an absolute light switch again. It's more like a dimmer switch. We're trying to head our best more in one direction or the other direction so if I'm just doing a recovery aerobic base-building day I'm not really going to want a huge ton of carbohydrates in my opinion around that time period but the context is important because then people carry that a little bit too far and they're like well I'm going to massively upregulate my body's ability to use fat and I'm going to start you know winning marathon events and well that doesn't work.

Danny Lennon: Right a couple of really important things that I'm glad that you touched on I think one when we talk about this idea of when we're at rest being in a state where we are oxidizing more fat in comparison to carbohydrate is pretty much universally a good thing. I don't think anyone would majorly disagree with that fact that when were at rest oxidizing more fat is a good thing and that condition that you mentioned when if someone is burning through a ton of carbohydrates when they're not doing anything when they're simply at rest that's pretty much how we would think of someone who's metabolically inflexible right and I think what this really gets at the point that hit me as you were discussing this and where maybe some of this misconception comes up is when we're thinking about how do we increase fat oxidation people thinking in the acute term as opposed to the chronic term and so there's things we can do to ramp up fat oxidation right now in terms of a meal choice we might have but that might not necessarily extrapolate out to in the long-term or chronically that person having good metabolic flexibility. Is that a fair assessment and would you add to that?

Mike T Nelson: Yeah and that's where it gets complicated right because if we look at the muscle and we take insulin sensitivity at the muscle level as a marker we can screw that up by not having much movement we can screw that up by different disease processes like Type-2 diabetes. We can also screw that up by a massive fat overload also so which is kind of surprising to people. So you can make someone very metabolically inflexible by just overwhelming their system with way too many calories. So even in some very high fat diets you can screw up the insulin sensitivity there. Now I think that gets into another argument of is that a “good or bad thing” so if you take an extreme approach like a ketogenic type diet you can also have what's called a non-pathological insulin resistance at the muscle level sounds like a whole bunch of mumbo jumbo but what it's saying is that in a ketogenic diet we know we have very high amounts of fat, we have a moderate-ish protein may be lower by fitness standards and very low carbohydrates usually dietarily less than 50 grams sometimes even less

than that. So it makes sense in that case that the muscle would not really want to use a lot of carbohydrates because the brain is controlling all of it and the brain says yes I can run on some ketones especially BHB, Beta hydroxybutyrate but I still like a lot of glucose and I don't want this pesky muscle taking up all my damn glucose. So if I make the muscle and it becomes more insulin resistant I'm going to spare glucose probably for the nervous system and the brain. So that's considered a non-pathological case. It's not necessarily from a frank disease process or a pathology but it's changing how fuels are used in the body in a different way.

Danny Lennon: Yeah I think that's just incredibly important to grasp in some of these conversations and I like how you frame that where when you take a case like a ketogenic diet we that state that's induced is essentially a state of insulin resistance. Now I like to say not in a pathological way but this transient way where it make sense that we don't want to be taking up all this glucose from our bloodstream if we have a limited amount and sending into muscle cells it's a in that case it's what that state demands but it's interesting how some of that gets missed when there's conversations around what a ketogenic diet will do for example for someone's metabolic flexibility at that time.

Mike T Nelson: Yeah. So to me the biggest thing I see with the ketogenic diet and metabolic flexibility is so and you've been around for a long time. You see all these progressions as they come through and fasting kind of came in and kind of went out and then ketogenic diets I saw kind of come in and kind of went out and now they're super popular again. I started looking at metabolic flexibility 12 plus years ago no one knew what the hell I was talking about. I didn't know anything about it so I just happened to you know literally fall into a lab that was looking at it and guys like David Kelly had been doing it since the late 90s [Indiscernible] [00:19:51] the crossover theory is in early 90s and well before that and the progression I've seen is it now metabolic flexibility is becoming more of a hot topic. We've got some and it's sort of if I'd say maybe blow-back against the ketogenic diet and so now people are like oh we need a cyclic ketogenic diet. We need to add carbohydrates at specific points and we really want to get to metabolic flexibility. So we'll have a ketogenic diet increased metabolic flexibility and they got like half of the equation correct. So if you look at the fat use end of the spectrum it is actually much more variable than I what I think most people appreciate. So study from [Indiscernible] [00:20:38] study that I did was posted in JSCR [Indiscernible] [00:20:43] took a bunch of people off the street hooked him up to a metabolic cart and under low-level exercise when they were

fasted the amount of fat that they're using as exercise was a massive variation from like 20 to like 93% difference meaning that some people are just really good at using fat some people are not very good at using fat at all. Again it's usually the fatty acid oxidation that's the limiting factor. So if you do a ketogenic diet it is correct that you will up regulate your body's ability to use fat as a fuel. So Jeff [Indiscernible] [00:21:22] faster study actually rewrote the textbook on how much fat you can actually use in highly trained individuals who were given fat, who were doing kind of a higher to still moderate intensity exercise. So everyone kind of jumped all over that and said oh great ketogenic diets increase the metabolic flexibility look at all this increase in the body's ability to use fat but what they forgot about is the carbohydrate end of the spectrum. So if you have someone on a very high fat diet for a long period of time or even just a couple days you start to see changes in an enzyme called PTH. So Pyruvate dehydrogenase which in essence is just kind of the you think of it as a gatekeeper to glycolysis the kind of gatekeeper to how well your body can use carbohydrates and you start losing part of that carbohydrate end of the spectrum. Now it's not massive I mean it's in like the single digit percentages so if you're not a super competitive athlete you could argue it probably doesn't matter a whole lot but if you're using this to perform better and especially at a higher level if you're a competitive athlete you start losing you know single-digit percentage off your speed and power that's a big deal. So I think a lot of the ketogenic people kind of got the left end of the fat burning-ish spectrum of the and correct but they forgot about the carbohydrate into the spectrum and last point one on that is if you've tried to switch in and out of ketosis like using like a [Indiscernible] [00:23:00] like ketogenic diet in my opinion it's just brutal. You feel like crap like most people unless you're extremely advanced don't switch out very fast at one study from Jacob Wilson's lab I think showed that they try to have him do a ketogenic approach Monday through Friday and it was like Thursday before they were back in ketosis Saturday and Sunday was a very high carb up type thing and I believe they showed some muscle loss in there too.

Now again that study has some other flaws and some issues and of course like all things needs to be replicated but I think again you just have to know okay this is a tool and why am I using it, here's the pros oops and here's also a con that goes associated with it. If you don't care about you know a couple percentage off your top end speed and power not a big deal no worries but if you're trying to get that advantage then it does become a massive deal.

Danny Lennon: Yeah and I think some of it goes back to what you touched on earlier Mike in that if we are looking at this from a perspective of metabolic flexibility it's not just looking at how much fat can we burn at rest it's also looking at can we get not only a burn carbohydrate at the right time but the ability to switch back and forth between those which kind of gets into this idea with the ketogenic diet at least within the sports nutrition that's sure where you'll have some people discussed this glycogen sparing ability whereas I think it's like Louise Burke [PH] and her lab have talked about well maybe it's actually glycogen impairing that you can't switch and start using carbohydrates effectively when you need to. What are your thoughts on that whole area and what kind of conclusions have you came to?

Mike T Nelson: Yeah that's – it's really it's a really good question and then you can make arguments on both ends of spectrum and I think we also have to be very specific about what approach we are actually doing and in what context are actually being tested right. So if we step back then they go okay we're going to look at marathon runners. So pull most people office street they go yeah use lots of fat not so much right most of data we have shows that highly competitive marathon runners are burning almost entirely carbohydrates. You know if you saw like the new world record that just fell he's running in [Indiscernible] [00:25:28] can't even do like a 200-meter at that pace. It's insane I mean it's just phenomenal that's almost all of carbohydrate use. Why? Because the speed and the power is so high now granted they can sustain that for an incredibly long period of time that if we block that and just had them only run on fat the speed the performance is just not there. So by energetically from a speed and power and the rate at which you can produce ATP fat cannot compete with carbohydrates where I do think some of the fat use is an advantage is if you have someone who maybe is not as competitive and you can push up their body's ability to use fat to a much higher level because we know that is trainable that crossover point has some flexibility, some plasticity in it that is a benefit because if you can use more fat yes you're missing out on some speed and power but you've simplified a lot of stuff right. You don't probably need exogenous carbohydrates to the same degree you probably don't have as much GI issues all the other things that come with that. So going back to your question about is it useful or not my gut feeling is that if you're trying to look at a flexibility approach based off of switching from a high-fat diet and then adding carbohydrates back in I think because of the PDH enzyme changes it's an access issue. So some of the studies of progression they did back in the 80s was hey let's just get fatty acid oxidation super high. We're going to create some you know freaks run

marathons. No that didn't work. So they are like wait a minute okay carbohydrates. They need carbohydrates. So let's do this metabolic flexibility thing that sounds cool well fat adapt them and then right before or two days before the race we'll just give them a piss-ton of carbohydrates. Now we've been trained and used fatty acid oxidation higher and they still have enough glycogen on board we're going to create freaks this is amazing. Well it didn't work and then they're like wait a minute maybe we didn't give them enough glycogen. So let's do it again let's do a muscle biopsy let's verify the glycogen stores are as high as possible. They did. It didn't work. And they are like wait a minute what the hell is going on and that's when they realized when the PDH enzyme changes they actually have pretty good levels of glycogen but it's an access issue to basically use them as a fuel. So the analogy [Indiscernible] [00:28:09] has made which I love is imagine you've got this huge gasoline tanker truck that's pulled over on the side of the road because it ran out of gas. It's not that there's no gas there. There's plenty of gas in this massive tank that is transporting. It doesn't have access to it. So I think in the context of higher fat background I think it actually is an impairment in an access issue not so much a substrate issue. So then the next question is well how do you get around that. So if we want let's say metabolic flexibility for an athlete does maybe just a baseline of health let's get rid of performance for a second and we want them to use a fair amount of fat but we still want the ability to use carbohydrates can we do something where we don't seem to have that impairment of the PDH enzyme and it appears that a time of intermittent fasting will actually do that. So if I have an athlete that say does 19 hour fast on Monday and I have them do some aerobic base building type stuff fasted in the morning I can come back Tuesday and give him you know 300-400 grams of carbohydrates they can store the carbohydrate, they can still access a carbohydrate, we can do a higher intensity maybe more speed and power work on that day without a seemingly an impairment.

Now that may be because it's such a short time period it was just the one day maybe it's because muscle glycogen probably wasn't used all that much because we didn't do just a piss-ton of muscular work. Liver glycogen can be lowered. Muscle glycogen is generally only tapped by the amount of work that's being done. So what I would like to see is if we can increase by using fasting the fatty acid oxidation end of the spectrum and still preserve that carbohydrate end of the spectrum as we prolong erasing it longer and longer or if we look at health parameters my bias is I think

that would be beneficial because we're trying to get kind of best of both worlds at that point without any interference between them.

Danny Lennon: Awesome. Mike I do want to turn from the performance side of things to specifically some related focused on health because I think there's a lot to cover with this and I think there's some really cool research going on in this area looking at metabolic flexibility, the potential role then of metabolic inflexibility in many of the metabolic diseases that we see now and I think even it's been kind of linked with some things related to immune metabolism and even chronic diseases like cancer and so on. So when it comes to metabolic inflexibility or what is driving that when we have something like these health issues that's associated with is there a kind of what is setting the stage for someone to become metabolically inflexible in the first place and then off the back of that what can we do to either a prevent that or reverse that once that's kind of established.

Mike T Nelson: Yeah that's a good question and in the case it probably comes to most people's minds would be like Type-2 diabetes. So I would say Type 2 diabetes everyone goes carbohydrate metabolism issue and I would say at a high level yeah probably generally correct but I think what they forget is that if you kind of go through what the body is doing so let's say for whatever reason you have a very poor time using carbohydrates at a basic level insulin is going to start to go up and glucagon is going to change there's a whole bunch of other downstream changes and then simultaneous changes have happened but for just the sake of a simple argument if we pick one of them insulin will start to go up the body says hey we can't have a lot of blood glucose hanging around in the blood it's extremely tightly controlled I basically have about 1 teaspoon of blood glucose floating around and almost any one point in time so we need to get this stuff out of here. I don't care put it in fat cells, put it in muscle cell just get it the hell out of here and so insulin goes up and up and up because the muscle or the fat or whatever tissue we're trying to deposit it in is becoming very resistant. I think it's probably becoming resistant because it's got a whole bunch of issues it's trying to resolve and it doesn't want it for various reasons as a self-protective type thing but the separate argument. So our baseline level of insulin we know goes up higher and higher but what happens then, well we actually start losing the ability to use fat as a fuel right because higher levels of insulin does not allow us to kind of downshift into the use of fat. So we get kind of screwed from the carbohydrate end of the spectrum gets kind of pushed more towards the center and then also over time and progression the fatty acid end of the spectrum also gets compressed on the other side. So it's a dynamic in my

opinion from both sides of the equation and I think that's what makes it a bugger to study because if someone is a Type 2 diabetic and is very metabolically inflexible you have to look okay was that on the fatty acid end of the spectrum is that on the carbohydrate end of the spectrum or have some marker for kind of the progression of that. [Indiscernible] [00:33:51] some PhD stuff we did this whole study with [Indiscernible] [00:33:54] department looking at some of this stuff and on paper I remember getting the labs back from these people and looking at blood glucose I'm like wow that person screwed oh my god, that person is really bad . This guy is not too bad he's high but he's not crazy high and then after the analysis came back I got the insulin to match it and the one guy who was high but not crazy holy Christ his insulin was sky-high. So looking only a blood glucose he'd be like huh he's screwed but he's not horrible and then when you see how high his insulin levels where you go oh my god that guy is a train wreck. So I think we need to be careful at what mark we look at and that's only excuse me looking at carbohydrates and looking at insulin. So if we extend that how do we get there oh man you can get there by all sorts of methods. You can get there by muscle inactivity. So we know a lot of the ability to just suck glucose out of the bloodstream is both insulin mediated and non-insulin mediated. So muscle contraction in and of itself can pull glucose directly out of the bloodstream. So we're giving our system a bigger sink to dispose of it and my bias is the more optionality you can have in that system the better. So if you can take it out from a health perspective and shove it into fat tissue like stick it in the liver, put it in the muscle those are probably relatively "safe places" to put it as opposed to it kind of backing up like in the sewer system into the bloodstream. So I think once those unfortunately those systems then start getting intolerant because of their own issues then it's going to start backing up. They're like hey we have this raging party going on here no we don't want 30 other people in our house. We're closing the door you know stay the hell out and then it starts kind of backing up from there. Dietary choices make a difference. Stress makes a difference. Sleep is a massive one that we have pretty good data on now. University of Illinois did some studies where I think it was five nights and they normally slept eight hours and they had him sleep four hours and they were basically borderline Type 2 diabetics at the end of those five days. Now that reversed as they got more sleep but these are like you know healthy individuals who'd just got crushed by not a lot of sleep for a week much less this being compounded over days two years and that's what makes it hard I think because people want what's the silver bullet, what's the what's

the one thing I need to do to prevent you know diabetes or metabolic inflexibility and there's a lot of things. Now the actions we probably already know more movement, more sleep, a different nutrition but the mechanisms on how all those are involved and how all they're all intertwined were just I think starting to try to figure out.

Danny Lennon: Sure and I think some of those things you mention are those kind of core big rock principles of being healthy overall but that kind of leads me into my next question or just thinking through and forgive me if this is based on some flawed thinking but given that we know that metabolic inflexibility is this kind of hallmark of many of these diseases when it comes down to is it almost a chicken and egg scenario of what is driving what or is that kind of dependent on the condition, is it that we can these things that lead to us becoming metabolically inflexible is a kind of precursor for developing more metabolic derangement which leads to issues or do we have certain disease states that develop on their own and therefore cause metabolic inflexibility, if that makes sense?

Mike T Nelson: Yeah I know it's the causation link right now which way does it go; is it one direction, is it bi-directional, is it again context-specific. I'm not a cancer researcher at all but you know from talking like you know [Indiscernible] [00:38:13] Andrew and other people that work in his lab my thought process is maybe different types of cancer have different types of metabolic flexibility profiles maybe like lifestyle factors promote you to become more metabolically inflexible. My current thinking is that it's probably from all the data we've seen bi-directional meaning that I think a lot of times in science we get really hung up on what direction is kind of causality and everyone poo-poos association it's an epi study it's only association and I get that and that on one hand makes sense but we know that if you have a horrible lifestyle we'll just bracket that as a whole bunch of stuff your body tends to become more metabolically and flexible. If we do things that are more healthy then you tend to become more metabolically flexible right. Your inflexibility goes down. We can do other things that will also make you very metabolically inflexible but there will be a cost associated with them. So if we take the carbohydrate end of the spectrum you can look at McArdle's disease. McArdle's disease they're missing an enzyme that does not allow them to break down muscle glycogen. By all measures that we've seen they tend to be generally healthy which again we'd have to define that term but if one of your markers of health is I'd say aerobic capacity which we know is associated with longevity lower body strength grip strength aerobic capacity vo2 max higher intensity exercise they do horrible at because they can't use

carbohydrates to run that. I do wonder about the health of some endurance athletes I've seen on a metabolic card test getting back to we talked about earlier on or man they don't even switch at all to using fat almost ever or some of the people I had come in the lab when I was there their fasted they're doing a low-intensity work they just barely got on the treadmill and there RER is like point 0.9, 0.95 right almost a 100% carbohydrate use and they're still running aerobic metabolism because you can run fat and you can run carbs aerobic metabolism and by what we know now most people wouldn't think that's not that big of a deal but to me that just seems really scary that your body is switching to a different substrate because it's needing to spin ATP at a fast enough rate. So I would love to see like a max aerobic test on those people because it's probably not very good. If we look at cardiac metabolic inflexibility or the progression of now heart failure and there's different ways to get to heart failure but everyone kind of agrees now that it's the change and substrate that is associated with it. Now we don't know which have you chicken or egg we don't know really which happens first but we have seen it can go both ways. So I think we're starting to unravel a little bit but I'm not sure if any of that really helped at all.

Danny Lennon: No, I think it there's a lot of good stuff in there and I particularly like that when you led with that to some degree at least for a practice it's probably not a great question to be asking anyway because as you had said in your previous answer if you look at some of those things that drive a lot of these chronic health issues and you look at the things that tend to drive metabolic inflexibility they're pretty much the same in a lot of cases and so if you have a poor health or you are metabolically inflexible then just doing those things is going to be helpful regardless of whether you are targeting improvements in health which will then fix metabolic flexibility or targeting metabolic flexibility which in turns improves health. So to some degree it may not be even a useful question for at least individuals to be worrying about. One thing that did pop into my mind Mike is when we're talking about metabolic flexibility is that tissue specific in that do adipose tissue and muscle tissue are they influenced differently when it comes to this or is it very much the same? Is there any differences based on any that type of stuff?

Mike T Nelson: Yeah you know it's something I thought a lot about. The data we have now would say it probably is both tissue specific and whole body specific. So for example so there's no real gold standard way of measuring metabolic flexibility either which makes it harder. So for a long time they set up an insulin clamp study was the best way. So briefly you would go in they put

an IV in your right arm and put an IV in your left arm and they put just a piss-ton of carbs in one, piss-ton of insulin in the other one and they're pushing you into a very a supra physiologic state and they're seeing how basically glucose and insulin kind of interact with each other and how high can we kind of push the system, and if you have issues there yeah you'll definitely see difference on a clamp study. The other argument has been that well that's such a super physiologic area that you're going to it may not be all that useful because it's not that representative but then other people would argue well what about exercise testing we put you on a max exercise test that's not really something you're doing every day either but when we stress the crap out of the system it gives us some pretty cool information we wouldn't find otherwise. That's why they do a stress echo test and not just one at rest or EKGs and things like that. So you could argue kind of either direction on that and in terms of like tissue specific so with the insulin one at the clamp study that's still a whole body level. Now you can take it a step now like what David Kelly did and you can try to run that across just like the thigh which is more muscle than the whole body. So they'll basically do an isolated clamp study across a muscle belly. You can go a step down and do some basically [Indiscernible] [00:44:58] testing looking at cells from diabetics both fat cells and muscle cells and we kind of see it show up at every level of the system. So my argument is from a usefulness not necessarily a research standpoint if we can show on a metabolic card at a whole body level that you're very metabolically inflexible now at least have a marker and we can kind of screen people to see who is at a higher risk because it may not be associated with body composition and you can also do that as an intervention. Alright, we're going to put you on this program here. You're going to work with Danny. You're going to do a lot of cool and nutrition stuff. He's going to have you exercise, maybe work on some sleep and then you're going to come back to the lab in eight weeks and we'll rerun this metabolic flexibility test. Maybe your body composition didn't get better. Maybe you don't feel a lot better but maybe we can show that from this health marker that we agree on is a marker of health of your system oh look you actually are getting a little bit better. So that's when I do my PhD work that's what we were trying to ascertain it's a non-invasive way that we can do that. We were trying to look at fine scale variability within the RER on a breath by breath metabolic card. So I think from that standpoint I think that to me makes the most sense. From a research standpoint right because now you're trying to be very mechanistic and figuring out okay what's going on all that research is very system specific and I don't think

we understand how it all kind of acts together. So one thing I looked at for body [Indiscernible] [00:46:43] stuff I'm like hey so can we just make the insulin just more in or the fat more insulin resistant because at a really high level what we don't want anything to be shoved into fat because of looking for body comp can we put it somewhere else and I finally found a rat study where they did a knock out model and they did just that they took the rats and they made their fat tissue only be via a different receptors very insulin resistant and what they saw was it was a disaster. They got massive amounts of triglyceride build-up and I believe they got like a non-alcoholic fatty liver disease. So I had to go somewhere I mean you think about it you're like oh that was kind of a stupid idea wasn't it because it's got to go somewhere. So my thought process on that is can we get it to go through so get glucose out of the bloodstream, get fat out of the bloodstream just put it wherever we need to and then could we have basically the engine big enough, the fatty acid oxidation big enough where it's just kind of flowing through the fat man we're just burning it out on the other end. So we get a health benefit and we also get a body composition benefit from it also. So maybe that would be one way looking at less tissue specific but an intervention and maybe in the future we can get very hyper specific to each individual system to see kind of what one is the the main point and the leverage point but I think we're pretty far away from that at this point.

Danny Lennon: Awesome. Thank you for that Mike and before I get to a final question I want to ask for people that want to dive more into this stuff and looking for more of your content where can they go online to get to some that work or to follow you on social media and any that type of stuff?

Mike T Nelson: Yeah sure. The best place is probably the website which is just MikeTNelson.com and at the top there will be a little GIF or way they can get out in the newsletter. So most the stuff I do now goes through the newsletter. So that would be the best way. If they want more information about the certification based on metabolic flexibility that's just a flexdiet.com, f-l-e-x-d-i-e-t.com yeah I'm probably on maybe Facebook more than anything else. They can probably just search my name and find me there.

Danny Lennon: And with that Mike I want to say thank you so much for the conversation today.

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