

VIDEO - Diet Doctor Podcast with Ben Bikman PhD (Episode 35)

Dr. Bret Scher: Welcome to the DietDoctor podcast with Dr. Bret Scher. Today I'm joined by Prof. Ben Bikman who is a PhD and associate Prof. of physiology and developmental biology at BYU. Now Dr. Bikman got his PhD in bioenergetics and he did a postdoc fellowship at Duke University in Singapore specifically in metabolic disorders.

He also worked for the company Insulin IQ and he is a scientist, he is a true scientist at heart, I think you'll appreciate that in this discussion. It does get fairly technical at times I have to admit because he does like to talk about the science and the specifics, but importantly we try and bring it back to how the science can apply to us as individuals in our everyday life. And you know when Prof. Bikman says something, you know it based on research, you know it's based on science.

And interestingly he came to the low-carb world through science whereas most people come to it through a personal experience, a personal connection and then start to learn about the science. He sort of came the other way and I think that makes him fairly unique but also fascinating.

So I love talking with Ben I love having scientific discussions with him and for you I hope you get a lot out of this from science but I hope you can take away some practical implications of what the science means and also a sense of Ben as a human being and how he lives his life by the tendance of keeping insulin low and how he helps to educate his family about that as well, but without crossing any lines, without being too overbearing with it.

And it plays it with the students as well and we'll talk a little bit about that. So a lot of topics, a lot of science but I think you'll enjoy this interview. If you want to get the whole transcripts please go to DietDoctor.com and maybe particularly useful for this one is we talk about some the science and some of the big terms and of course all the other wealth of information online at DietDoctor.com. Enjoy this interview with Prof. Ben Bikman. Prof. Ben Bikman thank you so much for joining me on the Diet Doctor podcast.

Prof. Ben Bikman: Dr. Bret Scher, delighted to be here, thank you.

Bret: We're so formal... Okay, we got the formality out of the way and now let's just cut to the more casual discussion here. So we are here sort of in your backyard, we're at Salt Lake city, you're associate professor at BYU.

Ben: That's right.

Bret: And you run a lab there, really focused on metabolic diseases. So tell us a little bit about your path, how you got into this personally and as a career path, to focus on metabolism and how that brought you to low-carb.

Ben: Yeah, you're right, so we are in my backyard. BYU is about 30 miles south of here in Provo and my lab at BYU is a metabolism research lab. And that has been an unexpected journey but one I'm so grateful for, sort of stumbling into this area. My undergraduate and Masters degree focused on exercise science and I was interested in the way fat cells-- My master's thesis looked at how fat cells are linked to inflammation.

And that was right on the tail of work coming out of Harvard in the early '90s, finding that adipocytes, fat cells, secrete pro-inflammatory protein, cytokines. That to me was mind blowing. The idea that the adipose tissue is an endocrine organ.

Bret: Right, not just a fat store... it's actually active.

Ben: That was the first I'd ever heard of that sort of situation. By that time I'd taken a gradual course in endocrinology, so I was familiar with the kind of stereotypical or prototypical glands; the thyroid gland, the gonads, the pituitary, the adrenal glands, these glands that existed in large part to secrete hormones that would have some systemic effect.

That study, I think it was in '94, finding that adipose itself can secrete hormones, well, proteins which are hormones in some instances, that opened up a whole new area of interest for me. And that to me it's started my interest in insulin resistance. So anyway, I'm being too long-winded but learning that the adipose tissue could secrete pro-inflammatory cytokines and that in that obesity associated, or induced inflammation, then could cause insulin resistance, that started my interest in obesity and insulin resistance looking indeed in that paradigm, obesity causing insulin resistance.

And then so I did my PhD work with a wonderful scientist at East Carolina University. His name is Linus Dome. And we looked at how insulin sensitivity changed so rapidly in people post gastric bypass. So it was kind of this disconnection in metabolic status. They are still morbidly obese of course one week post bypass surgery and yet they had

become very, very insulin sensitive quite quickly. I still think it's actually not more than just you basically starve the person for a week and look what happens.

But nevertheless I then followed that up with my postdoctoral work at Duke Singapore, that was more lipid induced insulin resistance. So my world was and still is insulin, insulin resistance and specifically making a research agenda that is focusing on the pathogenic side of insulin.

We talk about insulin like it's almost like a drug. You need insulin, here's your syringe. And yet there's a downside of course to hyperinsulinemia or when insulin is getting too high for too long. About five years ago... yeah... by this point... sort of started kind of moving into looking at ketones as independent signaling molecules. Just molecules in their own right, not metabolic garbage.

Bret: I want to get into all the specifics--

Ben: So that's how I got here.

Bret: So how did that translate to you personally, though? I'm curious, so that was sort of your academic journey into it. And then when did you start to internalize this personally and say, 'Hey, there's something to this, I want to start living this way'?

Ben: Yeah, that was probably about five years ago or maybe even a little more. About the time I started teaching my undergraduate assignment at BYU-- I teach pathophysiology and I wanted to devote-- so the sick body-- by this time the students have looked over the physiology, the organs, how the organs work within the body as a system. Now all these nursing and the premed kids come to me, they take pathophysiology and looking at how things are working when they are not working. And naturally I had a whole discussion focused on insulin resistance.

And looking at that point me... forcing myself to say... okay what is the best way to address insulin resistance? I'm a member of the American Diabetes Association of course, the rigmarole is, you know, whole grains, low-fat, high starch, pretty high starch and when I thought, I'm not going to rely on any textbook. I just want this to be a course that is based on primary literature... that's when things started to fall apart.

So I guess that's about eight years ago and it was maybe a year or so after that when I really appreciated the randomized clinical trials looking at low-carb vs. low-fat and I thought, boy this is all wrong.

I had always been healthy and I'd always elicited enough self-control just to stay lean and healthy, but once I really started losing my hair a while ago, unfortunately, I really thought to myself just from my ego's point of view, I can be bald or I can be

fat... I can't be both. You know, I knew I had to convince a girl to marry me and I thought, "Jesus, if I can just at least control how lean and fit I am, then hair be damned."

Bret: It's interesting, because you got there from an academic side.

Ben: Very much.

Bret: It has to be sort of disconcerting to say this is what all the textbooks say, this is what the guidelines say, but as an academic I want to see the primary research. And the primary research wasn't there to support those guidelines.

Ben: It was an uncomfortable adjustment because I now was challenging what I had been taught and told by people to this day that I greatly respect and admire as academics, if not necessarily scientists in certain instances, and that is of course a difference, you know, a professor versus a scientist.

But anyway, yeah, it was an uncomfortable growth, but it was not my personal experience in... you know, experiencing this incredible burst of health. I was already healthy, I was very active, eating generally pretty well even though on the wrong kind of direction, but still, like I said, manifesting enough self-control to avoid junk food which already put me in some pretty comfortable territory.

For me, my transformation was almost exclusively academic. It was-- which again, as an academic it made that transition both more uncomfortable because I thought I knew what I knew, but also gave me much more conviction because once I'd seen what I consider the reality, I couldn't un-see it. I could appreciate those P values for what they were. That statistical significance carried a great impact when I really found it.

Bret: Did you get pushback from other members of your department or at different society meetings or whatever that since you're going against the grain--? Although still based in science, did you get some conflicts or some pushback from colleagues?

Ben: I sure do... not for my department thankfully. And that's partly because my department has enough respect for me that the day will know even when they-- if they haven't overtly agreed with me, they can at least nod their head and say, yeah but I don't doubt that Ben knows what he is talking about.

But there are others, and in fact it's frustrating for me to even remember, there are others across campus in different departments who have been very upset with my perspective and have made life a little difficult. But for me it has always been, "Here are the data. Show me where I'm wrong."

Bret: Right.

Ben: One of the big points of contention was saturated fat should be no more than 10% of total calories. My sincere plea - here are a handful of clinical studies that put people on saturated fat diets that were up to in one study 50% of all calories coming from saturated fat. One actual randomized clinical study.

And here's a couple of other ones... please, prove me wrong. In all sincerity, please show me the study that number that the dietary guidelines are based on, that saturated fat should be no more than 10% of calories. Please, show me. Otherwise, leave me alone.

Bret: And there's no response to that, because that study does not exist and that's where a big part of my message is the strength-- the claim has to be backed by the strength of the evidence. And that's a case where it does not exist and you can say it's been a human experiment without going to the IRB to tell everybody to do a 10% saturated fat, because we don't have that study.

Ben: Now when I've been able to actually sit down with some of these people who've disagreed with me, almost-- I think not almost, without exception, it ends up being an amicable, friendly conversation and there can at least be a sentiment of let's agree to disagree, which I'm okay with, I really am. But when it is someone who claims to know what I think without ever actually talking, I don't have any tolerance for that kind of silliness.

Bret: That makes sense, but there's a lot of that out there, isn't there? Twitter, and social media and all over the place, people who just want to promote their belief, dig in their heels to defend their religion, so to speak, without really having an open mind to look at the other side and look at the literature and... that can be frustrating, I'm sure, for you.

Ben: Oh, no doubt.

Bret: One of the things you talk about are the plagues of prosperity.

Ben: Right.

Bret: I think maybe you coined that term, it's a great term.

Ben: Well if I did, I stole it from Gary Taubes, who had an article that he called Prosperity's Plague. So not to be-- Gary is far more eloquent than me, but I thought I can say that better. And so I said plagues of prosperity. Because in fact Gary was I think talking about diabetes and insulin resistance more tangentially and to me it really was all the modern-day diseases to varying degrees can have a connection,

have a common core. If it wasn't directly causing it, it was making it worse and of course that was insulin resistance.

Bret: Yes, so tell us about insulin resistance. It's a term that gets thrown around a lot and I've talked about before on this podcast that can be confusing for some people. Because insulin resistance, the cells are resistant to the effects of insulin, so insulin rises, so there's hyperinsulinemia. But there are also forms of insulin resistance with low insulin level. So what's a good way for the average person to think about insulin resistance and how it impacts their health?

Ben: Yes, so in fact, the way you described it initially is how I overwhelmingly look at the disease. It is a disease of-- as much a disease... at least when we think about the general systemic consequences, what it's doing to the body... It is as much a disease of... as insulin isn't signaling very well, so the resistance part of it versus hyperinsulinemia. You drive more insulin. In fact, I'm curious, you just mentioned there are instances when insulin is low and insulin resistance. I actually will very collegially disagree.

To me there are instances of what we call-- I've heard it in a low-carb community and I don't want to get us off on a tangent so you pull us back if we need to. People will sometime say you adopt a low-carb diet and develop physiological insulin resistance and I actually don't agree with that.

There are instances in human physiology of physiological insulin resistance and that's the two Ps as I teach it - puberty and pregnancy. But sure enough hyperinsulinemia, at least relative to what the person should be. And that's always a qualifier. If someone is normally going to be a four units, micro units, and there are 10, 10 could be in fact pretty reasonable for someone else. But nevertheless to me insulin resistance goes hand-in-hand with hyperinsulinemia.

And what we see in the instance of a low-carb adapted, fat adapted individual who takes a glucose load and now their glucose tolerance appears to be worse. In fact I call that glucose intolerance. Which is not the same as insulin resistance. And we are splitting hairs, but I actually still think it's important, because at least to me, I don't know... I'm not comfortable citing or invoking the term insulin resistance if insulin is low because if we were to give that person a bolus of insulin, that's going to work.

Bret: Good point... I see what you're saying.

Ben: If we were to infuse and doing insulin infusion, well, that glucose-- there's going to be a response to that insulin. And that's not the same as challenging the system with glucose, which I submit, the system has become somewhat intolerant to at least exogenous glucose.

Bret: So that just the fact that the pancreas isn't responding by increasing the insulin output for that glucose load means it's glucose unresponsive, not that the cells are resistant to insulin.

Ben: Yeah, right, but I can't say that I fully have my head wrapped around it, but I just don't like to-- I don't personally invoke the term physiological insulin resistance to describe the glucose intolerance that accompanies fat adaptation. To me they are different but I think it's important.

Bret: And that's the scientist in you.

Ben: But admitting that I don't know it all, more of the scientist in me.

Bret: So since we are talking about insulin there is this is balance between insulin and glucagon. So insulin the hormone that basically says we want to store fat, we want to take all the glucose and appropriate it where it needs to go and it's a marker that things are good, that we're in a fed state from I guess an evolutionary standpoint. And glucagon being sort of counterbalance the opposite of that. And so one of the things that I've heard you talk about before is this insulin to glucagon ratio especially how it relates to protein.

Because protein somehow has become very controversial in the low-carb world, that protein can trigger gluconeogenesis the new production of glucose, so if we have too much protein we can get ourselves into trouble on a low-carb diet. It's sort of a simple way to think about it and the science of it is much more complicated and paints a different picture. So that's a long lead-up to give you a runway here to go with, because I am curious how you want to explain this.

Ben: So the talk that I gave a year or so ago was the first time I'd mentioned the insulin to glucagon ratio and it was in the context of protein. Because as I had started that, I was still just a few months having stepped into the so-called low-carb community. I had I just gotten involved in Twitter for example and in the social media in general.

Up until that point literally three years ago or so I had no involvement whatsoever. I was studying insulin and even ketones a little bit in my lab and totally oblivious to this whole world. I'd heard the sentiment... hearing people adopting low-carb diets and their obsession with... drinking oil, literally drinking oil.

People that were getting hundreds and hundreds if not over 1000 calories per day in oils added to their drinks and I thought that is not healthy. And hearing this fear of protein, that brought me back to a concept that I'd kicked around and thought about years prior - the insulin to glucagon ratio. You said it perfectly and George Cahill was

the first researcher from decades ago who really looked at starvation and a lot of insulin.

He has a study called Physiology of Insulin in Man, this big beautiful review paper, it's so well done just to a quality of writing, etc. that you just don't really find. And I can say that there is a guy writing and trying to copy George Cahill... but he mentioned insulin as the fed hormone like you said, the hormone indicative of the fed state, but also the hormone that generally directs metabolism.

And what I mean by that is it directs the use of energy like you mentioned a moment ago is energy going to be stored or used or as I had introduced a couple of years ago or wasted and that's of course ketones. But nevertheless the insulin to glucagon ratio does give an overall reflection of is the body in a fed or a fasted state. The higher that ratio is getting the more it is indicative of a fed state. In other words store.

And inhibit so-called wasteful processes, like autophagy for example. And that's just a low hanging fruit when you talk about the opposite of the fed state which is fasted. Fasted state is a low insulin to glucagon ratio and the most obvious form or effective of fasted state is autophagy is enhanced.

And so when I was thinking about how to structure a conversation about protein I thought, let's look and see what happens in the insulin to glucagon ratio. And there was some delightful studies; it was kind of an amalgamation of studies but largely based on the work of Roger Unger from UT Southwestern. He's a glucagon guy, a legend in the glucagon research.

And his-- I found an old study from him which looked at the insulin to glucagon ratio and how the low-carb insulin to glucagon ratio was almost identical to the fasted state and several points lower than the conventional Western diet. So it was pretty interesting to me this idea of what I like to call a nutritional fast, rather than a caloric fast.

So someone who's still eating and getting energy and yet their body is still behaving as if it's in a fasted state. There's mobilization of fat, there's activation of autophagy, even though they're not in fact hungry, not fasting. So anyway, finding ultimately the protein, somewhat could eat protein... and if someone was in a state of glucose excess, like getting the protein at the same time as glucose or underlying hyperglycemia, that exaggerated this insulin to glucagon ratio. In other words, insulin really spiked.

In contrast, if you're eating protein in a fasted state or a low-carb state, because those two in fact are quite similar, then there was essentially no effect from the protein. And so I was eager to share that message when I learned it. I was enthusiastic

about it as well. But I have been delighted that insulin and glucagon, the kind of yang to the yin, have become kind of a part of the vernacular in the low-carb realm because glucagon is relevant.

I maintained the insulin is the hormone that has two hands firmly gripped on the steering wheel of directing energy but glucagon's got a hand there. But it is interesting to know the difference. Some people will eat protein and will in fact have massive glucose spiking effect. And it could be that if someone becomes a type 2 diabetic, their alpha cells, the glucagon producing alpha cells have become insulin resistant. That is in fact more work from Roger Unger, the glucagon scientist at UT Southwestern.

They found that part of what I like to say flips the switch from insulin resistance, which is hyperinsulinemia, but normal glycemia, flips the switch to go from hyperinsulinemia to hyperglycemia or over to type 2 diabetes, part of that is that the alpha cells become resistant to insulin's ability to inhibit glucagon production. So they become insulin resistant.

And that might be part of why the very insulin resistant type 2 diabetic or just in other words a certain amount of the population will in fact find that as they'd adopt more carnivore or more protein heavy version of the low-carb ketogenic diet, they might have some struggles with their glucose, they might have some struggles with insulin.

Bret: If they are already insulin resistant.

Ben: Yes, especially to the point of diagnosed hyperglycemia.

Bret: So we're talking a lot about glucagon here and it's probably unfamiliar for a lot of people, because it's not a blood test we do or their doctors do. So it was more of a research tool would you say and why isn't it being used clinically?

Ben: Yes, so you can get it measured, although I'm not the physician, but I know physicians who they do get it done. And there are general reference ranges, but it is a separate beast entirely, for reasons that I confess I don't know, something about the biochemistry of the molecule itself; it requires a totally separate vial of blood.

I know when we do what's called multiplex assays, we can measure or multi-analyte, we could measure insulin, leptin, cortisol, growth hormone all in one little batch of plasma from blood. Glucagon - uh-uh... it's an entirely separate test. It has its own set of chemicals that have to be added in order to isolate it and in order to quantify it. And again I don't know the reasons, but it's another beast.

Bret: I imagine-- I actually haven't looked into this, I have to admit, so it's probably something that not many labs do. It's going to be a send-out lab, it's going to be expensive--

Ben: Insurance definitely wouldn't pay for it.

Bret: But I think it would be helpful for some people to know, what is my insulin to glucagon ratio and would that affect the amount of protein I can handle? So short of having that test, what are some other markers people can use to try and help them determine if they can handle a certain amount of protein without worrying about gluconeogenesis, without worrying about their insulin to glucagon ratios?

Ben: Yes, that's a-- Bret, I don't know, there's not a-- I will say it if we can look at the insulin to glucagon ratio and maintaining it at a low state, as itself partly reflected by the insulin resistance state, then oddly enough the triglyceride to HDL ratio is a remarkably accurate predictor of who has insulin resistance.

But again we're making some connections here, then perhaps we could take that one step further to say it's probably a person who is going to have an insulin to glucagon ratio that isn't favorable.

Now one last comment about glucagon, as people are getting introduced to that perhaps for the first time, there is a phenomenon I almost hate to bring this up called glucagon resistance and that could be instances of-- when people have had liver damage like a hepatitis, like an actual infection. In those instances those are the very small group of people who-- and I emphasize this, it is a small group of people who genuinely have this, but that's when someone who might start fasting and things get very bad for them.

Bret: Interesting.

Ben: Because in that instance of glucagon resistance a glucagon's main action is to mobilize fuel. It wants to mobilize fats from fat cells, it wants to mobilize the glucose that's been stored as glycogen in the liver and it wants to tell the liver to make ketones, so it activates ketogenesis. In that fasted state the inability of glucagon to break down glycogen in the liver and to promote ketogenesis in the liver because the liver is glucagon resistant, makes for a brain that starts to suffer from fuel deficiencies.

So I have heard of-- I learned of this one person who claimed they would try to fast and they were healthy. And many people are so addicted to eating that they can't fast without it being very uncomfortable. That is not what I'm talking about at all. But this person, healthy lean individual that fast... and things really got bad for them,

profound headaches, extreme discomfort, they were able to find a physician who did a glucagon tolerance test. And this is documented in the literature where they inject a small dose of glucagon and then the expected effect is to see an increase in glucose.

Because glucagon will mobilize the glycogen from the liver. And this person didn't have it. So a failure to respond to the exogenous glucagon confirmed this glucagon resistance. And it exists, that is a real phenomenon, but albeit very rare.

Bret: Well, that's clearly the scientist in you; I see you get excited about that.

Ben: I was thrilled to learn something new, frankly.

Bret: Yeah, that's great ... So wouldn't apply to most people fasting, but for some people who do have trouble fasting, that can certainly be an issue.

Ben: And again there would have to be I think some history of a liver-- like an overt liver problem; cirrhosis, hepatitis, etc.

Bret: Yeah, alcohol or fatty liver. Now you mentioned autophagy a few times in the description of the insulin to glucagon ratio. So autophagy is a term we hear a lot about lately, a recent Nobel prize-- So give us a quick summary of what autophagy is, but more importantly what is the threshold for triggering it. Because I think it's such a controversial topic now.

Do we have to fast for five days to trigger autophagy? You know, is an 18 - 6 fast good for autophagy or is just low-carb good for autophagy? And how do we know? So give us a little rundown on autophagy.

Ben: Yeah, so as a general introduction, autophagy is a process whereby the cell-- I'm going to use this term and I hate to say it, but it kind of stays young. And what I mean by that what's happening... the cell is able to almost check its inventory and know that the pieces within the cell, what we call organelles, the mitochondria, the endoplasmic reticulum, the lysosome, the peroxisome, any parts of the cell inside of it, the cell can do an inventory and recycle those.

And so it's a way of keeping the cell regenerating itself in a way, keeping its function optimal, maybe that's the best way to say it. And thus people have looked at autophagy as a key to longevity that if you can promote autophagy, then your cells are going to continue to work better, regenerating themselves in a way and I'm not saying that they're resurrecting themselves, but just keeping themselves functioning optimally and that would logically lead to greater longevity.

In humans of course we don't have any evidence to confirm that, but that's a lot of the rationale behind the caloric restriction studies. Caloric restriction promotes longevity and that's not a sentiment I'm endorsing at all but that's the general sentiment. Calorie restrict... that promotes longevity and the intermediate event would be it's because it's promoting autophagy. At least that would be part of it. The truth of it is insulin controls autophagy. If insulin goes up, autophagy stops, because autophagy is wasteful. Insulin wants to store.

Autophagy is getting energy, it's catabolic it's breaking down parts of the cell. Of course it's in the effort of keeping the cell optimal, but it is still breaking stuff down; it is catabolic. And insulin is anti-catabolic and it is anabolic. Those aren't the same thing necessarily. Insulin is anti-catabolic in certain instances like at the muscle it is anti-catabolic and yet it is anabolic in other places like the adipocyte.

So nevertheless insulin very much controls autophagy. There are other variables too, but insulin is the elephant in the room. So once again we can come back to that insulin to glucagon ratio and essentially ask what keeps the insulin to glucagon ratio in a fasted state. Because if you are fasted you are activating autophagy.

Now like I said earlier according to Roger Unger's work from decades ago-- and in this is changed of course because we have higher sensitivity tests to determine insulin and glucagon now, but if I remember correctly the fasted insulin to glucagon ratio is around 1.5. If you eat a ketogenic diet your insulin to glucagon ratio is around 2.

If you eat a standard Western American diet it's about 4, so significantly higher. And so I can't say exactly where that cutoff is, but I would say if someone's keeping their insulin at essentially fasting levels, autophagy is running. Whether it's a caloric fast or what I call the nutritional fast, it's still going to be activating autophagy or won't be stopping it.

Bret: But we can't measure autophagy in people, can we?

Ben: No, we cannot. No, so there is... you only have these kind of surrogates, but I would strongly submit-- the insulin to glucagon ratio is a great surrogate. And maybe to keep it simpler, because it's hard to get insulin measured, of course it's even harder to get glucagon measured. If your fasting insulin is going to be around six and below, I would strongly submit that person has active autophagy.

Bret: Yeah, and that's really fascinating because for most people, they're stressing that there has to be a fast, that it's not just a nutritional method of keeping insulin low. That's a great perspective, you know, and again, we don't know one way or the other for sure, but it makes a lot of sense to say if insulin is sort of the controller then as long as you're keeping that at a low enough level, you're triggering autophagy.

Ben: Yeah and one important caveat there and that sets back to protein. There are many people who promote longevity diets and the whole schtick of the diet is restrict protein--

Bret: Restrict protein, yeah.

Ben: That's because protein is known to activate mTOR and mTOR is known to inhibit autophagy. That's their paradigm; restrict protein. So, eat these bars, drink this shake, it's very low protein, ah, but it's high carb. That's fine because it's protein that inhibits autophagy.

Bret: But what about insulin?

Ben: There was a wonderful study that looked at muscle cells, and it took maybe the most, if not one of the most mTOR activating amino acids, which is leucine; compared leucine to insulin and leucine and insulin both increased mTOR I think at the 15 minute mark, insulin did it higher. Here's insulin, here's leucine... For people who aren't listening, I'm going to describe it, I'm not going to pantomime with my hands. They both went up; leucine and mTOR exposure to the muscle cells. mTOR went up. At 30 minutes - the leucine treatment down, mTOR is gone.

Bret: Just 30 minutes?

Ben: It was already back down to baseline. Not the insulin, it stayed high and it went about three or four times higher mTOR activation, and it was maintained for about three times longer than the leucine. And so, the people who are pointing the finger at mTOR and implicating protein as the mediator, I say that's bonkers. Don't restrict protein which we know is necessary. And even though we have the same people who are poo-pooing protein, in their own human data they find, oh yeah sure, but when you get to 65 then actually if you eat too little protein, you die more.

That kind of challenges the whole longevity paradigm with protein being the villain. To me, if you want to control mTOR because you want to promote autophagy, well, then control insulin, and also acknowledge that we need to inhibit autophagy at some point we can't have autophagy constantly running in say our muscles and our bones. If so, they'd be always catabolic.

Bret: We'd waste away.

Ben: We'd waste away. So, you have to be able have these moments of activating mTOR, inhibiting autophagy, promoting anabolic processes. And so, even in that sense insulin is good, but protein is too, and I'm sure some people listening to me will be like, Ben, I'm not saying protein's bad, even though I'm studying it. But the more we

try to pin the protein as the culprit, the more we're missing the true villain, and that is insulin or hyperinsulinemia. If someone wants to activate autophagy and inhibit mTOR, scrutinizing insulin will give them a bigger bang for their buck than scrutinizing protein.

Bret: That's fascinating because that's a different perspective than we're hearing commonly right now. And mostly, we're hearing it from the vegan community or the vegetarian community because they tend to be more anti-protein, but in theory, on the superficial level, it makes sense.

Protein and mTOR, but as you were saying, insulin is the much bigger player, which brings into this sort of cyclical nature of an occasional five-day fast where you're limiting protein but you're also limiting insulin because it's a fast. But you don't want to do that all the time. Obviously it's very difficult to do and reset your metabolic rate.

So, are you a fan of sort of intermittent fasting twice a year, three times a year, that kind of thing? Or do you think a steady state of keeping your insulin low is sufficient, you don't need to do more for longevity, for health?

Ben: Yeah, yeah, so for me, personally, I don't enjoy multi-day fast. I once tried a two-day fast and I just did not enjoy it. Now, someone might say to me, Ben, you need to give it a few more hours and you'll get into that true kind of long running state. Yeah, but I just enjoy eating. And as a dad in a family, there's only so many days you can sit at the dinner table and watch the family eat, while you're talking to them, hoping your kids don't really notice.

And that's just something I'm very mindful of. I don't want to eat in a way that my two daughters especially, but that maybe sounds bigoted, but even my son would look at me and say, okay, daddy's not eating, so I'm not going to eat. And I am so worried about eating disorders, partly because I am a professor on a college campus and eating disorders are so rampant among especially young women at that age.

I'm terrified of somehow contributing to someone's eating disorder. But nevertheless, I enjoy eating. It's not something I enjoy going without. So, for me personally, I am a huge advocate of time restricted eating; 18:6 in particular. I will very rarely eat breakfast. I simply just don't enjoy it.

And I do my calisthenic body weight type workouts mid-morning and if I've eaten, I'm just more sluggish, I can't perform as well and I just don't need it, I don't need breakfast. So, these multi-day fast, I think they can absolutely have a place and I can deeply appreciate those in the low-carb community who are advocates of it. There's no question, there's an effect there. No question.

And I can look at that and nod my head and give them a thumbs up, but I'm not as much a fasting guy, I'm an insulin guy, and I'm thinking there may be other benefits of the fasting, like just breaking an addiction for food, realizing you don't have to have that when you think you do. But if I'm looking at fasting as a tool to lower and improve the insulin to glucagon ratio, which is in fact kind of how I look at things, I think there is a more comfortable way to do this, that is more sustainable.

Bret: Yeah, that was a great description, and I love you, the scientist, you know the science but also the practicality of it, and it has to fit into life and there's much more to consider with you as a role model, with you as a father, with you as a teacher, and promoting something that could trigger problems with eating disorders or sort of a body appreciation disorder. Yeah, there's much more to that.

So, that's pretty fascinating. And there's this whole world of are we promoting disordered eating by promoting a low-carb "restrictive diet". There are people on both sides of the spectrum. On the one hand, we're eating all the vegetables, all the meat, all the eggs, all the cheese. How is that restrictive? But on the other hand, in today's society it's seen as very restrictive.

Ben: It's frustrating, in fact just this semester, not naming names, so not disclosing anything, I had a student who approached me and said, "Dr. Bikman, it's uncomfortable for me when you talk about low-carb diets because it triggers my eating disorder." Now, first of all, if I could go on a tangent, I hate that there's been the birth in this generation of the term "trigger". For me, as a middle-aged guy, no one can trigger me, you know. You can say whatever you want to me. I am in charge of myself. You see my point?

Bret: I see your point.

Ben: I'll stop, so no one is triggering me. I'll pull the trigger myself if I want it.

Bret: Right.

Ben: But my frustration with that was-- first of all I was glad the student approached me, and as her professor I was very gratified and proud of her for doing that. But I was also very frustrated and I had to take a moment to clarify and I confirmed it was the student asking me not to show the data because that's all I ever do.

Here's a clinical study, another one, another one, another one. No, she wasn't. And it was the way I was talking about it. And I thought, well how am I talking about it? I do tend to be a very boisterous, somewhat rambunctious speaker, especially when I'm trying to keep my students engaged for two hours... I have a two-hour lecture period.

Bret: A long time for college kids.

Ben: Yeah, you're competing with Instagram and Facebook. So, you've got to be kind of clever about how you're talking about stuff, and so I did in fact very humbly and sincerely scrutinize the way I talk about things and thought, maybe I can be a little more respectful. But on the other hand, and I asked the student this; I said, "Have you had similar conversations "with professors who have been showing data or talking about low fat diets? Because if you're telling me this--" mind you I was very respectful and polite.

But I hated the idea that it was only the professor who was talking about a low-carb diet that was triggering an eating disorder. And like you said a moment ago, when I show these students the data, what is the common theme of these studies is that it's calorie unrestricted. It's the antithesis of starvation. It's don't count your calories; eat as much as you can until you're full and then you're done. It's glorious.

It is not calorie counting. And to me, that is the crux of so many genuine eating disorders like anorexia or even bulimia. It is "I can't get that calorie into my system, I need to restrict the energy". So I rage against that idea and I really hope in fact the very students, or anyone who's claiming that's an advocate of a low-carb diet-- mind you, when I'm in professor mode, I'm not advocating anything, I'm just showing the data.

And I kind of end up getting lumped in as an advocate simply because I'm the only professor who's showing it. And I do find I have to be a little more heavy-handed to make up for all the professors who aren't.

Bret: Right, right, it's true. I mean even if you are science-minded, which you definitely are and sticking to the science, you still need a louder voice to overcome the hundreds of other voices that are telling the opposite.

Ben: So I kind of get branded a bit of a heretic, but in reality, I'm just trying to be quite open minded to all of it. I'm just the most open minded that I've looked at the other side enough to really appreciate it. Mind you, there are other - I will say this in defensive - my colleagues... there are several other professors who feel the same way I do, many of whom because they've personally experienced the incredible metabolic benefits of it.

These are guys who've lost phenomenal amounts of weight and they just find they can't help but talk about it because they're so enthusiastic in a way and I'm not even, They have a conviction that I don't, because they felt it, I never really felt it, I just had the academic conversion.

Bret: Right, yeah, so you're unique in that sense where you had the academic conversion, whereas most people have the personal conversion and then look into the academic conversion secondarily after that.

Ben: Yeah, but you can understand. I think you've probably had the same kind of growth where there was more of a genuine, show me the numbers and holy smokes, this isn't quite what I thought.

Bret: Right, for me it was more seeing it worked in my patients and then looking into the evidence and then realizing it's not as clear-cut as it was being portrayed and then, like you said, once you open your eyes you can't go back.

Ben: You can't un-see it.

Bret: You can't un-see it, exactly. So, one of the other things you've talked about is ketones as a specific marker, as a specific effect on our bodies. And I guess there's a little bit of a debate which some would say it don't matter and some would say scientifically it absolutely matters. Is it just lowering the carbohydrates that give a lot of the benefits of a low-carb diet or is it actually the ketones themselves having an active role in our body and playing a beneficial role?

Ben: Great question.

Bret: So, tell us about the science behind that.

Ben: What a great question, and I feel qualified to answer it because of my growth. As I sort of told my academic background at the beginning, I really had come into this conversation academically, professionally through the lens of how can someone best control their insulin.

And that's what got me looking into and scrutinizing low-carb diets as a legitimate intervention and what I now still consider to be the most effective way, calorie for calorie, to control insulin. Lower the carbohydrate, I mean it is so rational. So, my perspective... my paradigm had been how can insulin stay as low as possible?

And then I was seeing, as I started to look through the human clinical data studies that would refer to ketogenic diets. And I of course knew, I'd had nutritional biochemistry... I knew what ketones were, but because I'd had nutritional biochemistry as a student, I also didn't appreciate them because they are not talked about in any way except negative.

Bret: Right.

Ben: In classic academic settings, ketones are more than just "metabolic garbage", they're looked at overtly harmful molecules that should be avoided at all costs. I mean, it is overwhelmingly a negative connotation to the ketones.

Bret: Right, we're only taught about ketoacidosis as a life threatening condition. And not about anything beneficial.

Ben: What a tragedy, and I mean it; truly, what a tragedy, especially when you look at it in the context of diseases like Alzheimer's or genuine instances of glucose hypometabolism although this is a tangent. But we know that in Alzheimer's disease, the brain cannot use glucose as well.

We're just about to publish a paper looking at gene expressions from different sections of the brain, human brains post mortem, looking at glycolysis genes in brains... of normal brains vs. brains with dementia versus ketolysis, the ability of the brain to use ketones. Whether the brain-- dementia or not, ketolysis gene expression perfectly normal. Glycolysis gene expression, not at all.

And I'm talking about P values of 10 to the negative nine. I mean these are massively beyond any hint of coincidence. Dementia brains have a compromised ability to use glucose, and we know this in human studies looking at glucose tracking to the brain, radio imaging. And sure enough, if the brain can't use glucose, there's only one other fuel, that's the ketone.

But anyway, our fear of ketones means people don't want them at all. But back to my story I would see in these low-carb studies some calling it ketogenic, and I would kind of look at that with a little bit of a grimace and think oh, ketones are bad, so I don't want to study that or I don't want to look at that study.

But more and more realizing or appreciating insulin's firm control over biochemistry that ketogenesis is an indicator of controlled insulin, and that was my initial appreciation. I thought, alright, if someone's in ketosis, it simply means their insulin is low, and that's a good thing. So, even then, firstly I was looking at ketones as no more than an inverse indicator of what insulin was, because if insulin is low, ketones are elevated. That was it for a while.

And then I was starting to see more and more of these studies being published, looking at how ketones improve contractility of the heart, for example, greater ATP production, so the actual molecule that can allow the muscles to contract, more ATP production per oxygen consumed. Think about an ischemic hypoxic heart; there's less oxygen and it can maintain ATP production.

So, the ketones improving heart contractility, ketone reducing oxidative stress in neurons. And I was seeing this, and I thought, you know what, I want to step into that. And the greatest beauty of being a scientist is freedom - if I have a question, I can ask it. And if I see, do I have the tools to answer that question?

So we started asking some of these questions. And to this point, we've published the one paper looking at how ketones improve or reduce the oxidative stress from muscle cells and maintain increase, enhance muscle cell survivability. So they're more rigorous, if you will, more resistant to insults. And so, that was a paper that we published last year.

We were finally wrapping up our paper looking at the way ketones affect mitochondrial function in fat cells, you know, that's kind of like the browning of the fat--

Bret: Making fat more metabolically active.

Ben: Yes, by several times, by multiples. We have another study looking at how ketones affect memory and learning in brain, with some very clever brain studies we're doing. So, anyway, to your point... to your question rather, I think the vast majority of the metabolic benefit that comes from a low-carb diet is that the insulin is controlled. I really do.

Now, it might just be that I'm the man with the hammer and insulin is the nail and I see it everywhere, but even still, I maintain that lowering insulin is the main metabolic benefit. The ketones provide, you know-- 80 % of the benefit of low-carb is from insulin control. The ketones provide the next 20 %.

Now, mind you, the more I'm learning about different molecules that you're eating from high starch foods there could be other factors, oxalates for example, and that's stuff I don't really know enough about. That might be a sprinkling in there, but to me, it is mostly controlling insulin.

Bret: Yeah, and it's a very important question because an issue that comes up all the time is do I need to be in ketosis? When is this low-carb good enough and when do I need to be in ketosis? If the ketones have more beneficial properties on their own, that's more to go into ketosis, but like you said, sort of 80-20. You get majority of benefits by going low-carb for most people, with a little added benefit by going into ketosis.

Ben: I would say that's true. Unless there's an overt like pathology, with dementia, with migraines.

Bret: Or if you're already diabetic or if you need more rapid weight loss then the ketosis will probably be beneficial faster. But for a lot of the sort of average people, low-carb is good enough with a little added extra if you're in ketosis.

Ben: I think that's a way to say it.

Bret: Yeah, that's an interesting point. We've talked about a lot of different subjects, a lot of science but you've already referred to your role as a family man, your role as a father, and that's sort of your primary job, your primary role. It can be difficult when you talk about food as a family, as a role model, as how do you feed your kids in today's society.

I know a lot of our listeners have kids and probably wrestle with this. So, tell us some of the strategies and things you use with your kids to help them learn about health, to help them learn about nutrition and to be that role model for them.

Ben: Yeah, yeah. In fact, Bret, thanks for bringing it up. Without a doubt, when I'm lying in my bed at night, I'm not stewing over my decisions I made at work, you know. That's such a small part of what I'm... not worried about but thinking about. It's family. It's about my relationship with my wife, my relationship with my children, that is priority number one. I'm aware enough to know that at the end of my life, I'm not going to regret if I wasn't in the lab enough, you know.

That's not going to be my regret. Yeah, so for me... the low hanging fruit in my wanting to impress upon my children the importance of what they eat, it is that I talk about fat and protein as wonderful things. And I don't really give them opportunities in the house to get away from that. We don't have cereal, they never eat cereal for breakfast, ever.

We don't have bread, we don't have sandwiches for lunch, we don't have crackers. That's just not part of the snacking system. It is little pepperonis, it is cheese sticks, vegetable platter with some non-seed oil ranch dip, you know. We make a ranch dip out of ranch seasoning in whole fat Greek yogurt, or sour cream, my wife does that.

Anyway, I will tell them, depending on what kind of food they want, I'll say, how can we have a little fat here, a little more protein? I want my kids someday to go away to college and when they're living with their roommate and open the fridge they'll see skim milk and they'll say, "What's skim milk?" Or they'll see low-fat free yogurt.

Bret: Why would you want to take the fat out of the yogurt?

Ben: I want them to be so stumped and befuddled that there is a significant part of the people who are afraid of fat. I want my kids to know fat is their best friend, and

protein is a close second or maybe it goes hand in hand. But essentially, my wife and I have been able to - mind you, it's still such a battle - the kids want junk food.

Bret: And they're going to get it at their friend's house, they're going to get it at their grandma's house or at their uncle's house.

Ben: Exactly, and you just can't get away from that and so they're going to put up fights. I don't want anyone to hear me and think that Bikman's kids skip down the stairs in the morning ready for bacon and eggs. No. Doesn't matter. I've been feeding them bacon and eggs for years. They'll eat all the bacon and they'll just pick at their scrambled eggs and I'm looking at them thinking, eat your bloody eggs!

You know, so that's the reality, it's far closer to the reality. It's not like my kids will just delightedly go grab a cheese stick. No, no, maybe one of them will and another one will complain about it and say, well, I want this.

And I'll say, we don't have that, we just don't eat that. And maybe someday it'll backfire, maybe someday they'll get out of the house, but they'll also know that they're healthy and they're fit kids, they know that. And they know that mom and dad are healthy and fit and some other moms and dads aren't.

Bret: Right, I think that's an important point and it's kind of hard to bring up in a politically correct way, to say look at us and look at some of your friends' parents and compare us. It's a hard thing to say and probably an important lesson when you travel, when you're in the airport and you see like a slice of humanity and how heavy everybody is.

I'll never forget when my son was maybe five at the time, he asked, "Is that person really sick?", because was talking about a very heavy, overweight person. I guess didn't experience all that much in his day-to-day life. He says, "Is this person really sick? Why is he so big?"

And then... it's a hard conversation to have with a five-year-old but I was sort of pleased that they understood that that's not right, and there's a reason behind that--

Ben: It's a delicate conversation to have, and for me... I'll try to focus on the positive, which is, like I'll joke with my son and my daughters too, I'll try to be as strong as possible, I'll say look at daddy's arm... When I flex my muscle, see it. It looks like the egg... This egg is helping daddy to be strong. Do you want to be strong?

And they all want to show off their muscles, or wherever, but I'm a terrible example, of course, I'm a pretty teeny guy. But I just want them to focus on the positive. I don't want to scare them into eating - if you eat this way, you're going to look like that

person. It's just rather, you've been blessed with a healthy, strong body, let's keep it that way.

This is what I want this healthy strong body, for me, daddy, mommy wants a healthy strong body, we are trying to do this by eating these kinds of things. So, they know it, as much as they might fuss about it. They will want ice cream. If I let them ice cream, they'd eat it all the time of course.

They're not those kinds of kids that are going to be offered ice cream and say no. No, no, they'd eat it. But I want them to know that's on one side of this food balance, and when we indulge in it, it is a treat and we enjoy it and then we know however that it can't be maintained and it can't be every day.

Bret: Yeah, good point, good perspective. So, tell us what a day in the life of Ben Bikman looks like.

Ben: Yeah, yeah, so I'll usually wake up, well lately I'm working on revisions for my book, that will be next year, it's just that whole kind of plagues of prosperity story. Which is we have all these fears of chronic diseases and we're treating them in all these distinct ways and there's another way of looking at them. Which is address one common core and now we can start addressing pretty much everything else.

I'll wake up around 5:30, maybe five, and work on the book a bit and then the kids will start to wake up at 6:30. We're very strict with bedtime. The six-year-old goes to bed at 6:30, the eight-year-old goes to bed at 7:30, the 12-year-old goes to bed at 8:30.

Bret: Oh wow.

Ben: It is written in stone. Mind you, they're not in their beds and lights out, but they're in their room, they potty, brush teeth, wash their hands. I mean that's that kind of rigmarole, we'll do a little prayer and then I'll read or whatever and lay by them and hold their hand for a long time. So it takes a while for them to fall asleep, but even still, they do and-- So, they start waking up at about 6:30.

I make breakfast, I'm in charge of breakfast, and we kind of rotate. It's bacon and eggs, it will be some egg muffins, some low-carb waffles made out of different kinds of whey and some different types of fats.

Bret: But you mentioned you do an 18:6, so you won't eat breakfast.

Ben: Right, what I might sometimes do depending on what I made for breakfast, I'll bag it up and take it to my office, but it depends. I don't personally like the low-carb

waffles that I make, but my kids do so I make it for them, and that would be something I don't eat and I don't bring anything with me.

So if I'm going to plan lunch for the day I'll either bring lunch; some cheese sticks, some meat, some hard-boiled eggs, which are a staple for me, or I'll make a shake. And I love putting eggs in shakes, just rocky style kind of shakes. Actually a shake that I'm involved in making called Best Fats, I'll put that in there with some eggs and that's my kind of-- that will be lunch and I'll keep it in the fridge.

And then dinner is dinner. Whatever the family's having-- Mind you, my family being what it is, it's never usually high carb it might be moderate, but usually it's pretty low. Or there's an easy way to make it low-carb but I'm not going to be too disruptive to the family. If we're getting pizza, the kids are going to eat it, I'm fine with it.

I'll usually eat the toppings and the kids know it and they'll tease daddy about it. But that's an easy enough one to do that's not too disruptive. I'll usually do my work out around mid-morning, depending on the time of year and the semester I'll teach on Tuesday and Thursday afternoons, but most of the time is writing. And then a little bit of time in the lab now with my students; I have enough graduate students that they keep the lab running independently of me and then I'm working on a grant or a paper, usually one of those two things.

Bret: Yeah. Alright, good slice of life from Ben Bikman.

Ben: Pretty underwhelming.

Bret: But I really appreciate that you are out there, that you are the scientist asking the questions Investigating to try and find these answers. And doing it from a science standpoint that you're not going to be the zealot promoting things above and beyond what the science says, you're always going to come back to the science.

And it makes you incredibly trustworthy. We know when you're saying something it's based in science, it's based in academics, and if we find a way to apply it to our lives, then it should work and make sense.

Ben: Right, well said.

Bret: It's a great perspective. Well, thanks so much for joining us and where can people find you to learn more about you?

Ben: Right, thanks Bret, for the invitation first of all and like I said, a few years ago I became active on social media. It is - I detest self-promotion blatantly, so it's never pictures of me, I don't like that for me personally. I try to share research, whether it's

my own research from my lab or latest published research, or even old research findings.

I am mostly busy on Instagram and Twitter and my handle there is benbikmanphd, and not so much on Facebook, Facebook's a little too overwhelming. But I consult with a supplement company, Unicity, which is great, and then I also have my Insulin IQ group.

Bret: Well, we look forward to seeing more research out of your lab and how your postdocs are working for you.

Ben: Thanks Bret.