

## VIDEO\_ Diet Doctor Podcast with Jason Fung (Episode 23)

**Dr. Bret Scher:** Welcome to the Diet Doctor podcast. Today it is my pleasure to be joined by Dr. Jason Fung, from the IDM program. Now Jason has been revolutionary in his use of intermittent fasting to treat obesity and to treat diabetes and in this discussion we cover a lot of that but we take it a little bit further and you get to hear Jason's perspective about how other diseases such as cancer, polycystic ovary syndrome and even little hints at longevity, how they can all be related to a similar process of too much insulin.

And we talk about where the levels of evidence exist for this and how we can kind of approach patients both with and without the evidence. I hope there's a lot of take home messages that you can take away from this interview to see how you can implement them in your lives, if you're suffering from any of these issues, but also sort of how to refrain this issue of insulin, its impact on our lives and our health and how we can implement fasting as a way to approach that.

Now, to be fair, fasting means a lot of different things to different people so we talk about the definitions and we talk about ways to make sure it's done safely, because that's very important. Just because something's good, doesn't mean more of it is better, and I think that's an important take home with fasting as well, doing it under supervision, doing it safely, can have a positive impact and that's part of what Jason has devoted a big portion of his career to.

Now, he's still a practicing nephrologist and that's sort of where all this started, but now with the IDM program he is reaching so many more people and spreading the word more about the benefits of intermittent fasting. So, enjoy this interview with Dr. Jason Fung, and if you want to learn more you can get the transcripts and you can see all our prior episodes on [dietdoctor.com](http://dietdoctor.com). Dr. Jason Fung, thank you so much for joining me on the Diet doctor podcast.

**Dr. James Fung:** Great to be here, finally.

**Bret:** It's great to have you. So, we already had Megan Ramos, who worked with you at the IDM program and talked about the amazing work that you and she and your whole team are doing, implementing fasting as a tool for metabolic health and reversing diabetes and weight loss, but it's not without its controversy is it?

**Jason:** No, I mean I think it's because of... it's really not been standard sort of for the last 20 to 30 years. Prior to that, people didn't care much right, but you know in the last 30 years,

everybody thought we had to eat, had to eat, had to eat-- to lose weight, you know and all this other stuff, so it has been controversial mostly because it goes against the grain. I mean, when I first thought about fasting, I thought it was a bad idea too.

And then you hear so much, like it's going to burn muscle, it's going to wreck your metabolism and don't skip breakfast, and all these sort of things that make it sound really scary, until you realize that people have been doing it for thousands of years.

**Bret:** Right and when you talk about fasting, I think the definition is really important because some people get in their minds that 10 day, 15 day prolonged fasts. It's mostly shorter fast that you're using in your program, isn't that right?

**Jason:** Yeah, exactly. So, in the 60s for example when people were doing all these studies, they would be doing like 30 to 60 days of fasting and you've got to remember these are not like obese people. These are people that had, you know, very low body fats because there just wasn't that much obesity and they're going on 60 days of fasting, it's like that's not a very good idea, and that's where people got into trouble like they shouldn't have been fasting, but they did it for some study.

I mean I look at some of these studies they did and they're incredible, like one of them for example, they had like-- I think they had nine people or something like that and they fasted them for like 30 or 60 days, then they gave them a big whack of insulin. It's like, I'm thinking why did they do that? And the answer was, "Just to see what would happen." So, they dropped the sugars to very low I think and it was like 1 point something in the Canadian unit so it's probably like 30 or something like that, it's ridiculously low.

And everyone was complaining they were asymptomatic, so you know these are the kinds of studies that no one would ever do, you don't do that kind of thing, it's you know you don't have to take those kinds of risks. So that's where people go more towards the shorter fast and there's no reason not to do them. And you've got to understand that fasting is a part of the normal life, like that's where the word breakfast comes in, you're supposed to feast then you're supposed to fast.

Well what's wrong with that? And you have a word that is actually part of your daily schedule, and now fasting for 12 hours is like insane, it's like everybody in the 70s did it like without even thinking about it. So it's sort of come all the way around that, you shouldn't even go like more than two hours without eating, it's like okay well, what about the normal nightly fast, right?

**Bret:** Yeah, and that's what makes interpreting the science of fasting sort of difficult, because depending on how you define it, it's going to depend on how you interpret the science. So, you and the folks at your program recently just published three case studies of some remarkable benefits with fasting, with people getting off their insulin and reversing their diabetes within

days, with fasting, but it was an alternate-days fasting with never more than a 24 hour fast in those three patients.

**Jason:** It's stunning. So, all three people, middle aged, they had between 20 to 25 years of type 2 diabetes, most of them 5 plus years on insulin and big doses, 60 units sort of thing, and it took a maximum of 18 days to get them off all their insulin.

**Bret:** So, a maximum of 18 days, that's incredible.

**Jason:** It was ridiculous how quickly they got better and the schedule we used, because we had to protocolize it somewhat, is 24 hours, three times a week. So, this is the thing that within less than a month they had significantly reversed their type 2 diabetes, even a year later, I think two of them are off all meds and non-diabetic by the classifications, you know by A1c and I think one of them was on some metformin still, but came off all the insulin and three out of the four medications or something, so doing ridiculously well for an intervention that is actually free, available to anybody and has been used for thousands of years.

So, it's sort of ridiculous how quickly some people can get better and you know as I was saying this is something that really needs-- people need to understand because it causes so much disease, type 2 diabetes, because I mean 20 years of diabetes, and we had just proved it was all completely unnecessary. Like do you know the amount of damage they did to their bodies with 20 years of type 2 diabetes to their hearts and to their kidneys, and to their eyes?

**Bret:** It was all completely preventable.

**Jason:** Exactly, like in a month they could have taken care of the whole thing.

**Bret:** Now in the case series they were following a low-carb diet in addition to the intermittent fasting. So, do you find the success varies with low-carb and without low-carb when you're instituting intermittent fasting?

**Jason:** Yeah, for sure we recommend low-carbohydrate diets for all of the type 2 diabetics, and it's really along the same lines. I think type 2 diabetes is largely a disease of hyperinsulinemia, so therefore both low carbohydrate diets and intermittent fasting, the goal is to lower insulin, as you lower insulin in a disease of too much insulin and you're going to get better, just like PCOS, if it's too much insulin you've got to lower it.

With type 1 diabetes, if you don't have insulin, you got to give it, that's how you're going to get better. So, it's not like the insulin is evil or anything like that, it's juts all context, like if it's too high you've got to bring it down, if it's too low you've got to bring it up, and that's how you're going to get better.

**Bret:** Yeah, a very simple perspective, but it can get a lot more confusing for a lot of people, they just need to realize the perspective there. So, the concerns about fasting are the safety of

it. So, one being your resting metabolic rate, is it going to go down with fasting and again time frame matters, doesn't it?

**Jason:** Yeah, for sure and you know if you're looking at some of the studies now so that nobody does these 60 day fasts sort of and studies it, but there have been studies of alternate day fasting and a lot of these are not true fasts so you have to extrapolate somewhat.

They are the ones that do measure resting metabolic rate, don't show any significant difference from chronic calorie restriction. In fact most of the studies and there is a number of them, so you have to kind of pick which one you choose, but most of them show that there's less of this drop in metabolic rate with alternate daily fasting and studies for example... one study where they did four straight days of fasting, their metabolic rate was actually 10% higher at the end of the four days compared to the day zero.

And again it all comes down to physiology because I don't know why, people get so bent out of shape. So if you don't eat, insulin drops, we know that, that for sure happens and when insulin drops, the counter regulatory hormones go up, we know that, that's why they are called counter regulatory hormones, they go counter of insulin, and one of the big ones is sympathetic tone, like that's not for debate, right.

**Bret:** So, sympathetic tone, you mean adrenaline, noradrenaline.

**Jason:** Yeah adrenaline-- so basically it's the fight or flight response. So if you see a lye and your sympathetic tone goes way up and you're either prepared to fight or run, really, really fast, your body actually increases growth of hormones, sympathetic tone or adrenaline, to actually bring glucose into the blood, it floods the body with glucose you can use to run away.

That's medical school physiology, okay so if you think-- and cortisol too, so cortisol is one of the counter regulatory hormones. So, if you think about it, okay so if sympathetic tone is going up, you know you're activating your body, that's what sympathetic is, parasympathetic, you're toning it down, but you're activating the body, what do you think that's going to do to your energy? It's going to raise your energy, it's going to increase your metabolic rate. It's like come on, this is medical school stuff, like why is this a debate.

And all the studies show that there's probably less effect on the basal metabolic rate from real world studies on alternate day fasting and stuff. Most of them allow calories and so on, so you have to interpret them a bit. It's like why do we worry about this? Where does this notion even come from? Because if you fast you're going to decrease you metabolic rate, that actually runs counter to what we all learned in medical school, of what happens when you don't eat.

**Bret:** With a one to three day fast, at least we can say that with pretty certainty.

**Jason:** Yeah, if you're going 30 days and 60 days, yeah you're talking about something totally different and almost nobody does that, like we generally don't recommend that either, I mean for us, we're like why take the risk. So, if you're doing 30 days, if you want to, it's great, but if you look at it, it's more powerful but there's more risk, so why don't you just do more shorter fasts? And that's the sort of trend towards where we've gone. So, in the 60s everybody's like, oh fasting is like a month right and it's like okay, fasting nowadays 16 hours is controvert.

**Bret:** Yeah, it's amazing how times change, and so the other big concern is lean body mass loss, muscle loss, nitrogen wasting and depending on how you measure it, it seems like you can come up with different conclusions.

**Jason:** Yeah, so again you can definitely measure nitrogen waste and then you have to say, is it muscle or is it not muscle? Not all protein is muscle, right?

**Bret:** So, I should actually clarify nitrogen waste, meaning sort of measuring the nitrogen in the urine that you urinate out and then the question is where did that nitrogen come from in the body?

**Jason:** Right, right, and I think it depends a little bit on what your perspective is. So, if you're talking about elite athletes, then it's something totally different than what I'm talking about for the most part which is sort of middle aged and elderly people who are mostly obese. So, there's a lot of excess proteins sitting there, so if you look at, again we're not talking about elite athletes, but if you're measuring it, there have been studies and they say that obese people generally have 20% to 50% more protein, than a normal person and that's all skin, that's all connective tissue, there's a lot of skin.

If you look at those programs where they have skin surgery, they're taking, you know like 40 pounds of skin, that's not fat, that's protein. So, there is excess protein, when you're talking in that specific sort of obesity type 2 diabetes situation, and you have to think that the body is going to maybe use some of that because that's all protein that needs to go. And again if you look at studies that have compared intermittent energy restrictions or IER versus CR which is chronic restriction and there has been a few, most of them generally show that there is less loss of lean mass as a percentage.

So one study from 2016 that was published in obesity for example, showed that you know you get about 0.5 increase in percentage of lean mass, because people are losing weight with chronic caloric restriction but it goes up by 2.2% in intermittent energy restriction or fasting. So you're preserving lean mass much better if you're using the fasting strategy, but this is sort of short term, 24 hours or less strategies.

So, again if you think about it, it's like okay, if you think that the body is-- when it has no food, it's going to bypass your excess protein skin connected tissue and go right for your heart muscles, it's like you must think that the body is really, really stupid. I mean, like honestly, you

don't eat for 24 hours and oh you're going to start breaking down your diaphragm. Like why would the body do that?

**Bret:** A muscle is a muscle, basically. So how does it know to target certain muscles and not others?

**Jason:** Exactly, it wouldn't. It's going to go for the stuff that's not needed and how would we have survived if our bodies were so incredibly stupid, that every time you don't eat, it starts breaking down your muscle, like let's think about this for a second. Like I do fairly regular fasting, so if I'm losing like quarter of a pound of muscle every time I fast for 24 hours, it's like yeah, I should have zero muscle right now. I should be this giant glob of fat. Instead, I'm pretty much the same, you know, composition as I was a couple of years ago when I didn't fast, it just didn't make any difference.

**Bret:** Do you recommend resistance training to try and stimulate muscle growth or maintain muscle during the fast, or do you think that's not necessary?

**Jason:** I think it's always good to do it, no doubt, but the thing about it is that the body is-- honestly the body is incredibly smart. So, if you put a strain on the system, it will respond by getting stronger, so muscles work like that. So you put a little bit of damage on your muscles and it rebuilds it to get stronger. You put weight on the bones and they respond by getting stronger. So if you look at astronauts, you take away gravity and all of a sudden their bones deteriorate like crazy, their muscles deteriorate like crazy. You put a man, hospitalize him and put him in bed rest only, which was the remember the-- five days of bed rest.

What you do is you take the strain off the muscles, so you take the stress off and you immediately start losing muscle, so if you want to lose muscle, that is the way to lose muscle, sit in bed all day. Like why would the eating have anything to do with it? Eating doesn't make you gain muscle, otherwise we would all be a nation of like you know Arnold Schwarzenegger's, right?

It doesn't happen, they are two totally separate things. You build muscle because you are working it, then you lose muscle because you aren't working it. If you're working it and not eating, your body is going to come up with a way to build that muscle, just the way it is, otherwise, again if you look at these Native Americans and all these people that used to go through these feast and famine cycles, and it was not like they were little globs of fat running around the prairies when the pioneers came.

They were lean and muscular and, you know, strong because your body responds to that, and I think it's really silly to think that our body is just so maladapted to life.

**Bret:** Interesting perspective, that the body knows, and we just have to listen and help it on its way. And then there are obviously a number of other issues about making sure that you're well

hydrated and have adequate sodium intake and reduce medications if necessary and I think that's a big issue of doing this on your own versus doing it with professional guidance. So tell us your perspective on that and what you're doing to help with that.

**Jason:** So, yeah that's our IDM program and it's basically to provide the education people need because it's not easy. It works but it's not easy, it's not fun, right? I would rather be eating donuts myself, but it's healthy and that's the thing, it is something that will improve your health, so you need to get educated as to what to expect. So, if you know for example that headaches are very common but they'll go away, you can deal with it. If you know that you're going to get hungry and there are tips that might help you deal with that hunger, then that's going to help you in terms of the fasting.

So, it's about getting the proper education and that's what we provide with our IDM program and also providing a support of community and that's is what is really the secret behind a lot of things, not just for weight loss, like Weight Watchers for example... they started out not with a diet but with those meetings, those Weight Watchers meetings and that's the secret sauce right? Same for Alcoholics Anonymous.

It's not like they didn't know to-- hey stop drinking. It was that you had a supportive group, a sponsor and that sort of thing. So doing it with a community is just way easier and that's the secret of how all these communities use to fast, they do Ramadan, hey everybody's fasting, hey it's lent, everybody's fasting, hey it's Yom Kippur, everybody's fasting, so it's not fun but it's as hard as it would otherwise be.

Because if you're trying to fast and everybody is telling you you're stupid and eating, like you know in front of you, that's not like the easiest thing to do, so don't you know you've got to set yourself up for success and that's what we hope to do for with the IDM program.

**Bret:** That's a great point and there's a lot of communities built around fasting that are sort of popping up so people can support themselves, and I think that's valuable. Now with fasting you can look at it from two perspectives, in terms of what you are treating. One is treating diabetes and obesity and insulin resistance and another is just promoting longevity and that's a whole other field of research. Now, with your book, *The Longevity Solution*, it looks like you've sort of delved more into longevity, so tell us a little bit on how the mindset changes when you're focusing on longevity rather than just treating and reversing a medical condition.

**Jason:** Yeah, that's a great question, I think it's really a matter of how to sort of maintain health throughout life and so then we looked in this book at a lot of sort of ancient wellness practices because I'm not about selling the latest supplement that's going to make you live forever, right?

I don't think that exists, but there are certain practices that have sort of withstood the test of time, that is they were considered to be wellness practices 2000 years ago and I think that has

merit because those practices have withstood the crucible of time, like if something is really bad for you and people do it, they'll like die out.

So, the fact that these practices or these foods or whatever have survived means that there probably is something and what's interesting is a thing that science is starting to catch up and fasting is one of these things and if you look at the science of longevity, the one thing that really stands out huge is calorie restrictions. That is probably the single most well studied mechanism for longevity in animal studies mostly.

But intermittent fasting is sort of a play on that and it is a way to restrict overall calories and maybe there's a better way to do it, but at least it's been used for a long time as opposed to sort of protein restrictions and or carbohydrate restrictions, those have not been used for as long. Intermittent fasting is a way to do that, and the physiology is... you know, a lot of these growth factors are also nutrient sensors and I think that this is a really interesting thing if you look at the theories of aging and why we age, or there's sort of, there's trade-off between growth and longevity.

Okay so if you look at a car for example, if you rev its engine, you can get high performance out of it, it's not going to last very long because it's just going to burn out. It's the same thing, if your body is growing, growing, growing like crazy, it probably does the same thing; it burns out quicker. So the growth program is probably at odds with the longevity program, because it's probably the same program.

**Bret:** And is part of that when you're triggering growth or stimulating growth, you're going to grow the healthy cells but you're also not going to be able to just limit it to the healthy cells, so potential cancer cell growth or abnormal cell growth will lead to chronic disease so we can't necessarily differentiate it.

**Jason:** Exactly because they're part and parcel of the same thing. When you look at the growth pathways for example, you have something like GF1, which is insulin growth factor one and so insulin, both insulin and like growth factor one are very similar and they're growth hormones.

So you can look at a population of Ecuadorian dwarves for example, called the Laron dwarves, and what was super fascinating is that this group of dwarves which-- they were persecuted in Spain, the inquisition forced them into Ecuador and of course there's this founder effect where-- because there's only a few of these dwarves and they all married each other, the small population, there's a lot of these-- this dwarfism occurred, and a few years ago it was-- when they were following these dwarves they realized hey these guys actually don't get cancer or diabetes either and then they're like, what's the difference between this dwarf and the other one. It's like they have no IGF1, it's like wow.



So, here's a you know-- the thing is if you slow down the growth program, then you might be able to age better, it all depends also on what stage of life; so if you're a child, an adolescent, you want that growth program running.

**Bret:** Right. Growth isn't by its definition bad. We need to grow, we need to build muscle which is part of health as well, but it's finding the balance, which can be tricky.

**Jason:** Yeah, but now if you're going for longevity, so if you're an average age of like you know, if you're in the middle ages, your average age is 30, then yeah it doesn't matter, you know, run that as hard as you want, it doesn't matter because you're going to die of the black death or something, right?

So it's like it doesn't matter but now if you're trying to get out to like 80 or 90 years old, you have to be a bit smart, so just like that engine, you can't run at full speed, you've got to cut back at some point though if you look at what stimulates growth the most, it's things like insulin, like growth factor mTOR and AMPK, which are all nutrient sensors and this is what's really interesting is that the nutrient sensing pathways are actually the same growth pathways because the body has to know when the nutrients are available.

**Bret:** So, nutrient sensors mean they're turned on or inhibited just by having nutrients in your body.

**Jason:** Exactly. So, if you like have an ovary for example, that's way on the inside, how is it supposed to now if there's food coming in? Well, it knows it because you eat, insulin goes up, protein, mTOR goes up, for example and if you eat fat AMPK is also, it goes down so those are nutrient sensors because it's the body's way of sensing if nutrients are available, and they are actually the exact same ones as growth.

So, now if you want to say, okay well this growth pathway after, you know age 30-- I don't really want to go full boar on growth because I want to live until 80. If you want now longevity, you actually have to cut down your growth pathway, which means reducing those nutrient sensing pathways, which is insulin, which is mTOR and AMPK, which is something that fasting does.

**Bret:** So, the question always is, where is the threshold for this, right, because again chronic caloric restriction can sort of lower the stimulation of it, you know the old saying, it may not make you live longer but it sure makes life feel longer. It's not as enjoyable to do. Yeah, so with the intermittent calorie restriction or intermittent fasting, where is that threshold and how do we know?

Because we can't necessarily measure mTOR and AMP kinase. It's harder to measure so we have to use surrogate markers, so what do you use as your guidelines to say here is where you're getting the biggest bang for your buck to do this level of fasting to help promote your longevity?

**Jason:** Yeah, that's a really good question and it really comes down to maintaining a sort of stable body weight and making sure you don't have the visceral obesity. Because the one thing we know of course, is that the metabolic syndrome is going to shorten your life, right.

It's going to give you heart attacks, it's going to give you all kinds of stuff, cancer and so on. And that's dependent on not body weight but waist circumference, type 2 diabetes and hypertriglyceridemia and all that sort of thing, so we know that those are all very important and those are obviously highly linked in to hyperinsulinemia and so on. So you're looking for a surrogate marker that's been clearly correlated to disease and that's going to affect longevity and all those things.

So if you are fasting and your weight is just way, way down, then yeah, you probably don't need to be doing that. But on the other hand, doing it so often might be something that is very beneficial and again if you look at it, it's like there's that sort of ancient wellness practice that people have done for thousands of years. Once a year, do a longer fast, just to sort of clean everything out, reset everything and then go from there, do you need to do it for longer? Maybe not.

But if you're 300 pounds and have type 2 diabetes, you probably need to be doing more, because you know that those insulin growth pathways are way, way too high. It's harder for mTOR right and that's really the tough part and we spend a lot of time talking about sort of optimal protein and stuff but that's really, really hard to measure because it's not as easy to see.

**Bret:** Yeah for something that's so hard to measure, mTOR sure gets a lot of airtime and a lot of discussion. And it's pretty controversial because we need it to grow, we need it for immune function and yet we can't have it, we shouldn't have it turned on all the time and part of that concern is cancer.

So this is another field you've been fairly vocal about, about fasting and insulin as it relates to cancer and that can be controversial as well because cancer, there's the one theory that it's sort of all of a genetic mutation and you know the drugs we're developing is high powered weapons so to speak to target specific genetic variations of cancer, and then there's the sort of the opposite side of a metabolic disease or maybe it's a combination of them both.

So, how do you incorporate that into your thinking and fasting in terms of cancer prevention or treatment?

**Jason:** Yeah, and I think that the cancer is a fascinating story. You know since I was in medical school we all talked about genetics, it was all a genetic disease right, it was just genetics, genetics, genetics and it's a mutation, it's genetic mutations, so if we can find the mutation, then we can block it, we're going to cure cancer of course, but that didn't happen.

So, we got the human genome project because it was going to cure cancer and then you had the cancer genome atlas which was an even more ambitious attempt to find out the mutations of cancer because we thought there was one or two mutations. It turns out there were like hundreds of mutations and not only mutations like between people, so one breast cancer cell to the next person's breast cancer might have like a hundred mutations and 100 complete different mutations on the other guy, even within the same tumor there are different mutations.

So there's mutations everywhere and clearly you're not going to develop 100 medications to block every single-- 100 different medications to block every single mutation, so that was sort of a dead end theory. And the other thing is, it's not about genetics, it's about the interaction of genetics and the environment, that we sort of forgot that it depends on the environment. So looking at obesity for example, the World Health Organization lists 13 cancers as obesity related, and including breast cancer and colon rectal cancer, sort of the number two and number three cancers after lung.

**Bret:** Which doesn't mean obesity causes these cancers.

**Jason:** No, it plays a role.

**Bret:** Plays a role and makes it more likely-- so sort of if you have a genetic mutation and you're obese, now the deck is really stacked against you.

**Jason:** Exactly, but now there's something you can do about it, because if you have a genetic mutation, there's nothing you can do about it, you have it, like I'm not going to change it, if you have it, you have it and I can't do anything about it. But I can change the environment in which that cancer cell lies because we know it's vitally important. You take a Japanese woman in Japan and you move her to Hawaii and San Francisco, the rate of breast cancer like triples, even though the genetics are exactly the same.

So what's the difference? The difference is clearly the diet and the environment in which that breast cancer cell is living, so again what is going to stimulate breast cancer cells to grow-- And in the lab the answer is very clear, insulin is what breast cancer cells need. You can't barely grow breast cancer cells in a dish without insulin. If you take away the insulin, they all like die. And if you give them lots of insulin, they grow, because the nutrient sensing pathways are the same as the growth pathway.

So you take this breast cancer cell, and remember the obesity didn't cause the cancer, but after that cancer cell is there, you're going to stimulate it to grow if you have a lot of insulin, so type 2 diabetes, a disease of hyperinsulinemia, higher risk of cancer, obesity, disease of hyperinsulinemia, higher risk of cancer, and then you say what about the other ones? What about AMPK for example... what blocks the AMPK or what affects the AMPK? Metformin.

It's like, oh well you know that metformin in a lot of studies has been associated with a significantly decreased rate of breast cancer and is it like the effect on AMPK, it's a very interesting hypothesis, what about mTOR? It's like because they are the three nutrient sensing pathways. Well, mTOR, you can block mTOR with rapamycin, which is an anti-cancer medication, right.

Why? Because you're blocking the pathways. So rapamycin is super super interesting because it blocks mTOR right. So, it's developed as an immune suppressing drug and the thing about immune suppressants, is that they generally increase the rate of cancer and the immune system sort of destroys cancer on site. So, if you give a drug that suppresses the immune system, like you give these transplant patients tons of drugs to suppress the immune system, cancer goes crazy and that's why--

**Bret:** Infections.

**Jason:** Infections, absolutely, but sort of unique amongst these immune suppressants, cancers went down, it's like wow.

**Bret:** The specific one - rapamycin.

**Jason:** With rapamycin, yeah it's like fascinating because you're blocking mTOR, so because you're blocking growth pathways, you don't have the-- that's why it blocks your immune system but it also blocks cancer, it very specifically targets this nutrient sensing growth pathway, which is the same thing, which is now a man humble pie. The diet... it's like... wow!

**Bret:** So, it's a fascinating field and one of the things that's important though is to talk about the level of evidence of support. So what you've been talking about is a mechanistic level of evidence of support and with the Japanese women moving to the United States, sort of the epidemiological or observational, so we don't know it was the diet, we know it was an environmental change in the diet, which is a big part of that and the mechanisms you're describing certainly make sense.

So it all seems to fit, but yet we don't quite have those human trials, to say yes it works which can make it a little bit uncomfortable for you to recommend fasting for that.

**Jason:** For sure, because you don't know what the effect is, but you know that for example if you use fasting to reduce obesity, you're a likely going to have a beneficial effect but you can't say that for sure. And the other thing is that we're, this is prevention right, so this is you talking, you don't know if you're going to prevent it because you don't know if someone's going to get it or not. You're not doing those big trials that are going to say we fasted sort of a million women and this is what happened.

Those trials don't exist so now we're talking about going into treatment and that's a totally different thing. One I don't think there's much data whatsoever but there is some super interesting data about sort of combination therapy, right. So, you say okay well diet is not going to cut it for a treatment, like you can't have breast cancer and think you're just going to fast and yes there's a few case reports and so forth but for the most part that is not going to work for most people.

But can you combine it with say chemotherapy to make it better? And that's something that's really, really fascinating because for example fasting reduces the side effects of chemotherapy. We know that because chemotherapy, and there's been a couple of papers on that, the chemotherapy affects the most rapidly dividing cells so in the human body the normal body, the cancer cells are growing faster, that's why you are targeting rapidly growing cells, the hair follicles grow quickly, the epithelial cells in the intestinal system for example are very rapidly growing so therefore you get nausea and vomiting and hair loss.

So, if you put these, if you now fast for 48 hours for example, and you get these cells to ramp down their growth, they will enter a sort of a more quiescent state, now you whack them with big doses of chemotherapy, you're going to get less side effects, so if you get less side effects, one you're going to be able to get a lot of treatments have to be ramped back, because there's too many side effects, so you would get the full treatment.

Or maybe you can get a higher dose treatment because you're looking for this maximal tolerated dose, and then there's some interesting data to suggest that maybe that-- So the worry there of course is that the cancer cells will also go into this protective state, but apparently some preliminary data suggests that this doesn't happen because they are stuck in this sort of on mode, that's the whole point of cancer that they are in this sort of growth mode.

**Bret:** They don't have the normal feedback loops so--

**Jason:** Exactly. For prevention you might be able to do something about it but for treatment, maybe you can combine it. And they talk about combining a ketogenic diet with drugs for example are going to be beneficial so they do these things so the PI3K pathway is actually the growth pathway, and they have drugs that can block it.

And they say what if you down regulate insulin by eating a ketogenic diet and then by giving the drug, like can you do better than doing either one alone. Those studies are very interesting, there's not a lot of data, so cancer is more of an evolving story that I think you know would be. You know, it's super interesting but ...

**Bret:** It's safe to say it's in its infancy but shows promise and so maybe in the next five to 10 years, we'll have a completely different discussion and say yes here's what the evidence shows, one way or the other.

**Jason:** The one thing you know for sure is that in the prevention you can prevent the obesity and you can prevent the type 2 diabetes and there is a good chance you're going to prevent some of these diseases. So remember colon rectal and breast cancer are the big ones in terms of obesity related cancers, because they have already been declared obesity related cancers, so with the idea that hey reducing obesity is going to reduce the breast cancer for example.

**Bret:** Yeah, that certainly makes sense. So, now transitioning from longevity and cancer to procreation and so you gave a talk today about PCOS, polycystic ovarian syndrome and you know you're a nephrologist, so you did mention, so what is a kidney doctor doing talking about the ovaries? So draw the line and connect the dots for us.

**Jason:** Yeah and I was saying that, I wasn't very interested in the whole disease until a few years ago when we started really treating people and Nadia who work with us at the IDM program. She was one of the educators and all these women are getting pregnant, like 15, 20 women have gotten pregnant, and I'm like whoa, that is really interesting and we've always known that PCOS, polycystic ovarian syndrome is related to obesity and the insulin resistance and type 2 diabetes.

So it was sort of part of that whole metabolic syndrome spectrum that I had been talking about, but I hadn't really looked closely into it and you know as I got interested I said okay let's look at what happens with it, let's look at the path of physiology, why are people getting PCOS. And it's been well worked out and I showed a New England Journal of Medicine review article that sort of spells it all out so under the influence of too much insulin, your ovaries start to actually produce a lot of testosterone.

And when you have a lot of insulin, the liver decreases sex hormone binding globulin, so the effect of the testosterone is increased because there's not a lot of globulin to bind it so the free testosterone is more active. So, therefore you get all the symptoms and the hair growth and the acne, clitoral enlargement, things that are sort of typical.

**Bret:** And the infertility.

**Jason:** Yeah, the infertility comes from the unovulatory cycles. So, you know, if you look at the insulin, what it does is it causes something called follicular arrest. So during the normal menstrual cycle, you have a developing follicle and then the sort of like the egg pops out and then it becomes a corpus luteum that involutes, that's a normal menstrual cycle. If it doesn't get pregnant, then you get the bleeding and the period.

So, if you have too much insulin, then you get follicular arrest and that means that the follicle stops developing at a certain point, so it never ovulates, it never reaches the size that it's going to ovulate and if it doesn't ovulate then there's no egg and you can't get pregnant. so that's another-- that's the infertility. And the thing is if it doesn't ovulate, it doesn't become the luteal body which then involutes, which means that it just sort of gets reabsorbed into the body.

So, you've stopped the follicular development at a stage where it doesn't ever go away, so you've got these cysts that develop over time. So, okay so those are the three sort of criteria of PCOS. You've got too much insulin which causes the follicular arrests which causes the cysts, you've got too much insulin which causes the follicular arrests which causes the unovulatory cycles and then you've got too much insulin which causes the hyperandrogynism.

So the whole disease is a disease of too much insulin and it's been well worked out and it's been in this review article... So it was like are okay... well like if it's too much insulin, then bring down the insulin, that's how you're going to make the disease better. That's the root cause treated. Instead, that's not how we treat it, we give drugs.

**Bret:** We give drugs.

**Jason:** It's like, oh, my God. This is a total replay of like type 2 diabetes. So, here you know the cause and you know the answer. The answer is if insulin is too high you got to drop it. How are you going to do that? Low carbohydrate diets, ketogenic diets, intermittent fasting. Instead we give birth control pills, we use Clomid, which is a-- you know, causes the ovaries to start hyper secreting and that's like, okay it's not the answer, right?

**Bret:** So getting mechanistically makes complete sense and now the level of evidence to my understanding is low-carb diets that can reverse a lot of the hirsutism, the hair growth, but I don't know if we have any evidence saying it improves fertility but yet there's lots of anecdotal evidence of that happening. Do you think we're going to bridge that gap so that this will become a more common treatment?

**Jason:** It depends if anybody is interested in actually looking at it, that's for sure, that's right. You know and this is one of the reasons they use metformin because they use it as a sort of, you know, insulin sensitizer, which makes a little bit of sense so I-- at least that makes a little bit of sense. But you know the question is who's looking at it, like these low carbohydrate diets haven't been used for a long time because we worry about the dietary fats.

And intermittent fasting hasn't been used. When I started talking about it like six years ago, like I was really just a lonely voice in the wilderness. Nobody, but nobody was studying this. So, are the studies going to come? I hope so. I don't know that there's a lot of people interested in it, but here's the thing and this is sort of the art of medicine as opposed to the science of medicine. Everything in medicine comes down to risk versus reward, so if you give a drug like a beta block or you do a stent or something, what's the risk of doing a stent? Because there's risk, because everything has risk, and what's the reward?

If the risk is more than the reward, then you don't do it. If the reward is more than the risk, you go ahead and plop in a stent, or you give aspirin or you give beta blockers or whatever it is. So, what's the risk if you don't eat, you know for 16 hours of the day. What's the cost like... zero?

What's the risk? If you are overweight, there's practically no risk, so then you say well okay there's no risk so any reward you can get is a plus and here's the thing, you don't have to prove.

If you're a patient with PCOS, if you're somebody with PCOS, you don't have to prove that it works in everybody, you only have to prove that it works in yourself. So, if you have type 2 diabetes, if you have PCOS or any of these diseases, you can simply say, I'm going to try it. I'm going to try it for two months because it's not going to cost me anything, I'm going to do low carbohydrate diets, I'm going to do intermittent fasting and see what happens.

If nothing happens and your disease is just as bad as before then you haven't lost anything, you can go ahead and just do it, but what if your disease completely goes away? Right, now you've done something that all the drugs haven't been able to do for you and the thing is that it's big money here. So IVF is big money, it's like four plus billion dollars a year, so these people who are doing fertility treatments and all the sort of stuff-- like if you ever go into one of those clinics they are really nice, they look like a spa.

**Bret:** Right and it's also miserable for the women, I mean it is so uncomfortable and difficult to do and it can all be changed potentially with nutrition, yeah.

**Jason:** Potentially, yeah, and it's not just the discomfort of the IVF, it's like if you want a baby, it's like you want a baby, it's like very totally like--

**Bret:** It's an emotional cost.

**Jason:** It's a huge emotional cost and the time is ticking because people are getting married later, we know that, people are having their babies' later. It's funny you know because, you know, my sister got married at like 22 and had her kids at like 24, she was like the latest of her friends.

**Bret:** Wow, right.

**Jason:** It's like nowadays people are getting married at like 35 and having their baby at like 38 or something like that right. So if you're having your baby at like 35+, I mean that used to be considered as low fertility time.

**Bret:** Right, that's advanced maternal age.

**Jason:** Exactly, because fertility sort of peaks around 20 right, like you can't stop getting pregnant at 18 or 20, right, but at 35 it's not as easy as it was, so if you're wasting time because you're like saying I got to wait for the evidence and you know I'm going to do cycles of IVF, it's well like why not, like you can do that. But why can't you add it to or just use it instead? It just makes no sense and that's what I mean, it's sort of the art of medicine, because it's not like do I not have evidence that works, no, but...



**Bret:** Yeah, it's a good perspective. We talk a lot about evidence based medicine and that is important to understand the quality of the evidence, especially when there is a risk to the treatment, like you're saying. So, I think that was a good perspective for you to talk about weighing the risks and the benefits is what we do for everything.

If the risk is very low then the need for evidence is also a little bit lower if there's a potential upside, it seems like one of those circumstances. Yeah it was sort of a whirlwind tour through the fasting, through longevity, through cancer, through fertility and it all tends to have a common theme, doesn't it.

**Jason:** Yeah, this is the thing, the thing is that we look at the-- and I went over this and the diabetes code is that-- if you look at the five sort of things that deal with metabolic syndrome, so the waist circumference, type 2 diabetes, high triglycerides, low HDL and hypertension, they're actually all linked to hyperinsulinemia, but there's actually so much more to it because it's like after the metabolic syndrome it's like obesity linked I think mechanistically really to hyperinsulinemia, type 2 diabetes, linked to hyperinsulinemia, PCOS linked to hyperinsulinemia, but also things like cancer where it may play not a sort of causative role but sort of facilitative role.

I mean you're talking about the biggest killers in America, so heart disease, stroke, diabetes, cancer are sort of like at least four of the top five and all of them are impacted by hyperinsulinemia. I think that's a better term than insulin resistance as it immediately tells you what you need to do. So, insulin resistance doesn't tell you what you need to do.

**Bret:** Good point.

**Jason:** So, if you say, I have insulin resistance, people will say what caused it, and then there's all this debate, oh maybe it's a high fat cause in insulin resistance, I don't think so, but if you say now, that the problem is hyperinsulinemia, then you say okay well I have too much insulin, bring it down. It's like well it seems pretty obvious how you can bring it down.

Cut the carbs and don't eat, so it's much more powerful. So just changing that word, makes it so much more powerfully clear to people, what you're supposed to do because there's been a shift in medicine, right. If you look at the causes of death, there's a complete shift from sort of 100 years ago and you're talking--

**Bret:** Trauma, infection.

**Jason:** Exactly, right, the infections and diarrhea, you now, that sort of thing to what are now, you know well the top two, sort of, if you're looking at the cause of death too and then there's everything else. Heart disease and cancer are off the scale in terms of the amount of people they kill and then everything else is actually quite a bit lower than that.

So, and those are diseases which are going to be impacted by metabolic syndrome and also we know cancer, like for so many years was thought about as a genetic disease, it's like what about the genetics when you put it in a high growth environment, which is a high nutrient environment, and it's like okay, well you know that cancer, you go back to sort of those traditional African societies and stuff.

They had cancer right, a lot of them were viral cancers, lymphoma and so on, but those cancers like breast cancer, they practically didn't exist. The Eskimo, or the Inuit that we call them now, in the far north of Canada, they actually studied them, very intensively to see why they were immune to cancer.

**Bret:** Immune?

**Jason:** They're immune to cancer, except for EBV they got nasopharyngeal carcinoma and stuff, but they didn't get breast cancer and they didn't get colon rectal cancer. And then of course, we took them away from their traditional lifestyle of hunting and gathering and gave them white bread and you know seed oils and sugar and all of a sudden cancer just goes way, way, way up.

So, we pretend that cancer is this disease of all genetics, genetics, genetics but it's not because two of the sort of-- okay if you talk about the big three cancers, lung cancer, obviously it's just smoking, right? Let's forget that. So the next two are breast cancer and colon rectal cancer, prostate cancer is number four and is actually very common, but doesn't kill as many people because it's slow growing and it doesn't sort of effect the younger groups as much.

So, breast cancer and colon rectal cancer, which we've already declared are obesity related cancer, so it's like let's face the fact that these are actually diseases that may have something to do with insulin and reducing a state of hyperinsulinemia might be highly beneficial for them, and again what's the downside?

**Bret:** What's the risk, yeah.

**Jason:** Exactly.

**Bret:** So, when done safely, that's the key. When done safely when fasting, with low-carb nutrition, when done safely can make a big impact with very little downside.

**Jason:** Yeah, absolutely.

**Bret:** Well, it was a great summary and a great discussion of all that, so thank you very much for taking the time. Give us a little hint, what's next for you and where can people learn more about you?

**Jason:** Yeah, so they can go to our website which is [idmprogram.com](http://idmprogram.com), which stands for intensive dietary management and there's lots of resources, free resources and paid resources if

you want more. You can go on Twitter, I'm usually fairly active there. I've got the books, you know. Next up, you know I'm writing a book about PCOS which is sort of you know about what we talked about and also, I'm doing that with Nadia and then also a cancer book as well.

Just talking about sort of, it's not like a how to cure cancer, because that's not going to happen, but it's sort of this, you know I'm really, really fascinated because the whole story of cancer has changed so completely from what we thought it was. We thought it was just a bunch of randomly accumulated genetic mutations and sort of from 1990-ish, you know when I went into medical school in 92 sort of to 2010 probably, it was all considered genetic mutations.

But now the whole theory of what cancer is has completely changed and now we're talking about evolution, using evolutionary biology and trying to understand how cancers develop and we're trying, talking about, you know-- One of the really fascinating things about cancer is why it occurs in every single cell in the body, like almost every single cell in the body can become cancerous, and that's really weird, and it's not just that.

Almost every multi cellular animal in existence can develop cancer, even a hydra which is one of the most primitive multi cellular organisms can develop cancer. So cancer is not a disease of just humans, it actually predates humanity by a lot. It's a much, much more ancient than we knew, and it actually probably dates back to the transition between uni-cellularity and multi-cellularity, which is, you know what is, and that's really what the fascinating story of cancer really is, and that's ...

**Bret:** That almost speaks against insulin resistance, as being a contributor, so I think it's more complicated than--

**Jason:** It's definitely more complicated. But insulin resistance or hyperinsulinemia is going to play a sort of facilitative role, it's going to make-- it's not going to cause cancer.

**Bret:** I think that's an important differentiation.

**Jason:** If the cancer is there, it's going to make it grow faster. That's the difference, you take a Japanese woman from Japan and she may get breast cancer but if you put her in a high nutrient environment, which is a high growth environment, that is give her lots of you know, bread and insulin goes way up and MTOR goes way up, well you know all of a sudden that breast cancer, which wasn't a problem, back then-- You take a look at the Inuit for example, they clearly have the potential to develop cancer, but they're keeping insulin so low for example that those cells never get the growth-- #!Environment matters.

**Jason:** It's the environment that matters but then you put them in-- you give them you know fried bread, which is basically like white bread fried in oil, that's what they eat. Now you give them a high growth environment and now those cells that would not have grown, do grow and that's when you start to see cancer.

So we go from a time where we consider the Inuit to be completely immune to cancer, these people don't get cancer ever, to hey they get a lot of cancer over here, and it's because of the environment, not because of the genetics. So, that is the sort of story of cancer, so it's not really just about fasting and so on, actually you know, I'm more interested in the deeper story which is changing and I don't think it's the end of--

I don't think it's the final answer, there's just so much more to be learned about it. But it's just very interesting as we move from that transition, from a paradigm of pure genetics to a paradigm of evolutionary biology, which to me is a much more fascinating.

**Bret:** Interesting structure change, for sure. Well, thank you for all your information and all you're doing online and all you're doing to help people and promote the idea that insulin matters and environment matters, thank you very much.

**Jason:** Thank you.