Opening on ketogenic performance findings

What we found is that when athletes were either on a ketogenic diet or on high carb diet, the ketogenetic diet did not produce any deterioration in physical performance.

Book promotion and podcast intro

And when we looked at what was fueling these athletes, fat metabolism made up the majority of fuel substrate during this activity at a level of fat oxidation that was higher than any fat levels ever reported in the medical literature.

Some athletes where over 1.85 grams of fats burned per minute during physical activity. Hey everybody, we'll get right back to the podcast, but I do have some very, very exciting news I want to share with you.

And that is that my new book, Brain Defenders, that we've been talking about on the Podcast is now available for purchase. It is going to be published in August of 2026, But it is available now.

If you want And that is oddly enough, brainedefenders.com. This is really empowering information as it relates to charting your own brain's destiny. Now let's get right back to the podcast.

Well, hey everybody. Welcome again to The Empowering Neurologist. I'm Dr. David Perlmutter. You know, for years we've been told that carbs are the indispensable fuel for human performance, meaning athletic performance.

That athletes must consume high amounts of carbohydrates to compete. to succeed, to recover, But what if that narrative is incomplete? What if the very strategy meant to optimize performance is quite compromising in terms of our metabolic health?

We're gonna find out that in fact it is. Today on The Empowering Neurologist, we're going to dive into the fascinating and potentially I think paradigm shifting conversation with Dr.

Dr. Kutnicku2019s personal story and type 1 diabetes

Andrew Kutnick. He is a metabolic scientist who synthesizes nearly 600 studies and challenges over a century of conventional sports nutrition dogma. His recent publication that appears in Endocrine Reviews, we're going to be talking about it, reframes basically how we think about fuel utilization during athletic performance.

How we think about things like fat oxidation, how we utilize fat as fuel and the whole notion of metabolic flexibility. And I will tell you that we're gonna take this conversation not just to the realm of athletic performance, but the full notion, of Metabolic Flexibility as it relates to our general health and even our long-term health, what it looks like to be metabolically flexible in terms of long-term health implications, even as it relates to the brain.

But certainly we will spend some time talking about how this information was derived from his evaluation of high-performing athletes. You know, if you've been following my work ever since the Grain Brain days, you know that I've long emphasized the role of metabolic dysfunction as being really a root driver of chronic disease, especially in brain related disorders.

And what Dr. Kutnick's research does, it extends this conversation into the world of sports performance. Then it brings it actually right back to body health, longevity, metabolic flexibility.

And he shows that this whole notion of metabolic resilience is not just for elite athletic performance, but really for all of us. So we're also going to explore something I think that's really quite important, and that is an area that he has

great expertise in.

Dr. Kutnick is a type 1 diabetic. and we're going to explore the efficacy and safety of being on a ketogenic diet long term as actually a therapeutic approach to type 1 diabetes.

That's a discussion I think that challenges the deeply entrenched fears that many physicians have in terms of using a Ketogenic Diet in type one diabetes And it also I think opens the door to a more personalized physiology driven level of care.

And this is a conversation about clarity, about moving beyond polarization and about understanding how metabolism truly shapes our performance and truly shaped our brain's destiny for that matter.

So thanks for joining us. Let's jump right into our podcast. Well, Dr. Kutnick, welcome to the podcast It's an honor, David. I appreciate you having me on here.

But I think you tell a much more empowering personal story. So let's open with that. And then we'll get right into your new article that you just published, project.

But first, tell us your personal stories, because I it's really important for our viewers to know really what makes you who you are. Sure, so I grew up in Tallahassee, Florida in the United States of America for those who are international listeners.

But as a kid, I started to develop excess body weight, you know, and a lot of that was fat tissue. It wasn't because of a lack of activity. Me and my friends would ride bikes regularly, play sports regularly.

We would do this every day for multiple hours per day, but I was still gaining weight. Uh, you know, we still followed many of the nutritional advice that was out there in the world at that time, but again, still gaining weight.

And, uh, eventually I was able to find some success by changing my dietary habits, and losing weight, But I actually did find myself as a kid becoming and being classified as technically obese.

I, was obese as kid, I struggled for five years to get weighed off, failed numerous times, really changing nutrition was, key to that. But it was actually a year removed from overcoming obesity.

that really my life truly changed forever, and that was with a diagnosis on a family trip with type 1 diabetes. This is a form of diabetes where the body no longer produces insulin, the most powerful hormone in all of metabolism, that changes arguably most other hormones, enzymatic processes, how the bodies essentially metabolizes the fuel from being storage-based to catabolic.

I mean, it really is the dictator between those two states in the body. And now, for the rest of my life, since I've been 16 years old, I have been having to manually inject insulin at every meal of every day and having constantly adjust due to the numerous variables in life including exercise, lifestyle, sleep, sunlight, heat, medications, and many others that ultimately change insulin sensitivity, sometimes not just day-to-day, David, but hour by hour.

So this really changed your perspective. You're 16 when this happens. How did that guide your professional career? Well, at that time I was obsessed with being bigger, stronger, faster.

Growing up as an obese kid, all I could think about was being the polar opposite of that. I would look at these bodybuilder magazines and see these super lean, very muscular body builders and think, I want to be that, and everything they would talk about And eating the right way and so I was very very focused on those factors in my life But really what was being uncovered at that time for me when having to manually administer insulin and also tracking glucose levels Essentially minute by minute throughout the day was a keen insight on how various forms types intensities of exercise various lifestyle habits the type of nutrition you eat that all the way down to the individual type Of foods you're consuming and how it all changes insulin and glucose levels on a very, very intimate level.

Every day I was essentially challenged with a new set of chess pieces on the chessboard, and I had to ultimately navigate to what amount of insulin would I need to administer, at what time, where should I inject this, ultimately to get the output in glucose that I wanted.

And this really created a unique learning experience where essentially all day, every day I was playing my own master of my metabolism. I had to understand very intimately as anyone with type 1 diabetes does about my nutrition, about how exercise is going to affect insulin sensitivity and all these other variables.

Many of these variables only came to light in science decades later. But people with type 1 diabetes have very much appreciated how various things like sleep deprivation impacts insulin sensitivity the next day.

How exercising can sometimes reset insulin-sensitivity after something like deep deprivation if it's sufficiently hard for sufficiently long. All these different things ultimately come together.

And it was actually that, David, that really pushed me to really want to understand very deeply how the body worked, ultimately to optimize my own health.

I got a PhD in biomedical sciences, I've got degree in exercise physiology because I wanted to truly understand how do I optimize by own how? How do optimize own performance?

And ironically along the way we ended up finding information that helps millions and millions of people do the same thing. So, you know, we talk a lot of the podcast about the effects of non insufficient sleep or poor quality sleep, lack of exercise, stress, various, certainly diet on.

how that plays out in terms of insulin sensitivity and ultimately glucose levels. But you really had firsthand experience in a very critical way of very acute changes measurable in your blood sugar from all of these inputs.

So who better to discuss with us these effects than you? You've gotten a front row seat in way that nobody else can. You know, I wanted to speak today about your new study that you published in just a couple of months back on just really kind of challenging our whole notion about the need to carb load or the importance of carbohydrate in the diet as relates to physical exercise.

Ketogenic diet as therapy for type 1 diabetes

But having said that, in getting ready to chat with you today, it did know, look upon a really, I think, fundamental part of your research, and that is this really iconoclastic way of portraying the utility of a ketogenic diet in a type 1 diabetic.

I mean, you know for medical doctors, that seems worrisome because we're always concerned about diabetic ketoacidosis. But what you're talking about, and let's unpack this, is the idea of actually and thoughtfully utilizing a more ketogenic diet, i.e.

less dietary carbohydrate, more dietary fat, that this can help regulate blood sugar and allow people to be less taxed by adjusting their insulin levels as did you, as you probably still do.

So let's talk about the day you decided to, you know, get, go to your computer and you're going to write a study, design a, study looking at the use of a ketogenic diet of all things in type one diabetes.

How does that all unfold in your life? So that also relates back to a personal story where I… Which is great. Yeah. I first was walking into my endocrinologist's office, who, by the way, was the American Diabetes Association president over a decade ago.

And he was an amazing endocornologist, pediatric endokornologists. After having switched my nutritional strategy, I'd heard that there's this diet where you reduce your carbohydrates, your body shifts from burning sugar and carbohydrates to burning fat, and it may, may spare muscle, although at the time it was being portrayed more like

magic.

It would keep muscle forever and then fat would just burn away. And to oblivion, I'm like, that sounds great, David. That sounds wonderful. Let me try this.

And so I had actually reached out to a professional athlete at the time who also had type 1 diabetes. and said, Hey, Andrew, here's the thoughts on this.

I just kept asking questions and questions. Then I started emailing them incessantly like, what do you think about this? Hey can I do this and eventually like hey Andrew like I can help you but we got to officially find some way to work together and so we did.

And this person essentially helped guide me through my own desire to understand switching onto a different diet mainly because I heard of its potential in body recompositioning and sports-related endeavors.

And so when I tried it, it was ironic. I actually got much stronger. Uh, I did lean out rather quickly. Um, but what was also fascinating, which is all things we now know and expect with, uh, ketogenic style approaches, we know now it's self-evident, right?

Yeah, essentially when people get on to a ketogenic diet, they're lowering their glucose, which causes a lowering of insulin. And essentially that causes the cascade of events which you drop water weight, so you essentially lose weight almost instantly.

Then by default, the evidence shows that people volitionally reduce their caloric intake so people can lose weigh on top of it. We won't get into too many details, but there's this cascade of things that happen from the first meal all the way over days to weeks and months on these diets that facilitate some pretty positive therapeutic effects for many individuals.

But for me, when I tried this approach, I remember walking into my doctor's office three months after I started. And I remember walking in and sitting down and he walks in, very unique character, a very, unique, character.

He walks into the room and says, Andrew, what are you doing? And what do you mean? What am I doing here? He's like, your HbA1c, which is a measure of your average glucose over the last two to three months, is that of someone without diabetes at all?

you must be doing something. And I just, you know, grinned ear to ear. I'm like, oh man, well, let me tell you about this diet I am doing. So I reduced the carbohydrates, I was focusing on protein and fat and green leafy vegetables, and I switched my insulin strategy to match these slower impact foods on glucose because protein does impact glucose, but it's very subtle and prolonged.

I want you to speak to my residents. I wanted to go speak at the local medical school. Because he was so fascinated, he had not seen this before. And so I felt extremely empowered.

Obviously, I'm doing better than Jim. But I also am finding myself not going through these sub-perceptual swings that I didn't realize I was going to at that time, David, until they were gone.

Until I found like, oh, wow, i'm not really going these highs and lows anymore. Every time I am checking my blood sugar, I'm somewhere between 70 to 120 milligrams per deciliter, which for someone, if we translate that, that's 3.9 millimolar to approximately, let's say, 5.6-ish milli molar for other units.

And so I just felt great. I then became obsessed. Obviously, nutrition has an impact on not only my weight and my obesity, but now it's having an ability to regulate an irreversible chronic metabolic disease where 99% of patients will never get normal metabolic control after their initial diagnosis.

But here I am. just making a different change in the grocery store with my lifestyle and all of a sudden I'm in that

1% that's giving normal metabolic control and it wasn't that hard.

There's got to be something to this and so this just drove my fascination to understand nutrition in general. as a therapeutic medicinal tool. I knew that for years I'd go into exercise physiology lectures when I was getting my degree and they'd say exercise is medicine.

They'd also say nutrition is a medicine, but I would see it firsthand in my own life that I struck with a disease where you're supposed to live 10 to 20 years shorter.

You're suppose to get at least one chronic complication of typically a retinopathy of the eyes, neuropathy in the nerves. uh nephropathy of the kidneys or you have tenfold higher risk for cardiovascular disease you're expected to get at least one chronic complication within your lifetime and deal with high and low variable blood sugars which are mental health symptoms fatigue irritability Um, lack of concentration, reduce cognition.

These are just normal daily experiences of people with type one diabetes. But here I was removing all of that away because I wasn't able to get normal glucose control.

So I became obsessed about how nutrition impacted metabolism, health, And performance, I went on to complete my exercise science degree. I was involved in research from 10 over research studies when I.

Was an undergraduate at Florida State University. Then I want on too, uh, look for various schools. Spent an entire year just looking around for where can I truly understand.

how food could be evaluated as a medicinal tool. And I had applied, I actually reached out to 60 different programs over that time. It was actually a very unique conversation with my wife coming to visit her in Tampa, Florida, where her roommate worked with a researcher named Dominic D'Agostino.

And she was looking at ketones and the, uh, this rare disease called Angelman syndrome, a neurological based disorder. And I was, and she said, why don't you just reach out to this guy?

He does exactly what you're fascinated about and been doing for your own personal life for, for years. Why don' you reach to him? And so I sent an email like almost midnight thinking he'd never respond.

I get a phone call. Yeah. But Dominic would, he is gentle giant. He is the true epitome of one of the greatest humans I've ever met to this day in my entire life.

He calls me the next day, David, and within 30 minutes, I show up at University of South Florida College of Medicine and I end up speaking to him for the almost two to three hours.

And it was that day forward I said, This is exactly what I want to do. I wanna use these tools, these strategies and understand the impact of food on health.

And that started my research career from that point forward where I worked at University of South Port College of Medicine for essentially seven years.

five and a half years for my PhD, I stayed on for a postdoc. I then went on to study through funding with the Special Operations Command, United States Government Department of Defense, to see how those same strategies we're looking at in disease model systems and brain cells and other cell systems, how they would translate to a human being in a performance setting where their life was on the line.

And then I went and ran research projects with the Florida Institute for Human and Machine Cognition, where we studied that in military settings. Then I want on to Sansum Diabetes Research Institute, right?

Went on study how we then translate these tools into chronic disease settings, were individuals aren't just trying to improve their performance one or two percent, they're trying improve there health 20, 30, 40 plus percent.

Metabolic flexibility and ketones in health

And my hope was to uncover tools and strategies for someone living with a chronic irreversible disease like type 1 diabetes where they could achieve the potential top 1% because ultimately that's the goal, David.

Any patient who's struck with chronic metabolic disease or even on their way to a chronically metabolic diseases, they want to go to the doctor and be told they have the opportunity to be normal again if they had the right strategy and we wanted to find that strategy.

Hey everyone, we're going to get right back to the podcast, but I have an important message for you. If you're caring for somebody with Alzheimer's, any other form of dementia or even what we call mild cognitive impairment, or maybe you've received one of these diagnoses yourself, Or if you are focused on preventing cognitive decline, I want to speak directly to you for just a moment about some serious research that's going on looking what we call 40 Hertz light and sound simulation.

We've been actually talking about that on the program. Here's the challenge. Not all 40 hertz light devices are the same. Most use what's called stroboscopic light, and that's type of light that flashes, then you can see the flashing.

And that can cause nausea, it can cost headaches. And if you can't tolerate that, you won't use it. So there is a company called Optosudix. They've solved this problem with a patented technology that still gives you the 40 Hertz light flashing, but through light that looks and feels quite normal.

It's the device I actually have on my desk when I'm working. And that's why this company sees a 94% adherence rate and significant improvements across various metrics, including mood, energy, focus, sleep, and memory.

And the light is called the EV light, EVY. You can use it as I do when you're working on your computer, when your reading, watching TV, eating breakfast, whatever.

It becomes really part of your day, not just another burden, it's kind of passive in the background. So I recommend giving it a try for 90 days. And if you and your family don't see value in it, then you can return the device for a full refund.

They cover the shipping both ways. You can learn more about Optosudix at optosüdix.com forward slash Perlmutter. you could use the code to get a $200 savings.

The code is Perllmuter, my last name 26. This is a device that really is risk-free in terms of getting involved with 40 Hertz stimulation. Important information.

Let's get right back to our podcast. I'd like just for our viewers to take a deep breath here because What we're talking about here transcends type one diabetes.

We're taking about the fundamental importance of how this hormone works in the body, insulin, and ways of augmenting that and actually stabilizing, not only that, but the other side of the equation, that is how our bodies utilize fat for fuel.

And that takes a little bit of work to transcend our body's metabolism into being a fat burning metabolic machine, as it were. It seems that in your 2025 paper that you wrote about that lowering carbohydrates and sugar ingestion was, I think you called it a centuries old approach for diabetes.

And yet with the advent, the Banting and Best discovery of the, or the ability to create insulin for human a utilization that this kind of fell by the wayside and that really what evolved from that is basically chasing your blood sugars without any regard to what you're eating but basically, chasing you blood sugar as you did with an insulin dosage and varying that insulin dose based upon what your reading and you were always catching up.

But I think what you're describing is kind of, I, think revolutionizing the whole notion of targeting insulin and its

functionality and metabolism. So, um, take it a little bit further though than the type one diabetic, because I know that you've spoken about this and I'd really like our viewers to know how central this role, how essential metabolism is and optimizing metabolism, Sure, I think the best way to describe it is actually to piggyback off of something you said, which is the manuscript you wrote up, Century Old Wisdom.

And why we called it that is because we know that in 1796, John Rollo was a physician who applied these tools in type 2 diabetes to reverse two patients with type two diabetes condition with lowering carbohydrates.

We know in 1860s that there was physician, who also um the Banting was his name or actually it was a it's a gravedigger uh uh in a who actually went on to self-administer a lower carbohydrate approach that was able to resolve his own obesity.

And so essentially these tools have been around in publications for preventing and reversing obesity and multiple forms of diabetes for essentially two centuries here, David.

We've known for over a hundred years that it's been applied to reduce the frequency and severity of seizures and epilepsy. We've known for recently its application in various neurological disorders with the emergence of pilot data and now meta-analysis and GMO psychiatry showing that these tools can be applied in settings like anxiety disorders.

schizophrenia, bipolar. That's a really fascinating situation where individuals were struck with a mental health disorder. And now we're seeing that it isn't just physical changes in how you look in the mirror.

It's actually changing the way your brain functions and operates, which we have known for over a century. But now, we are actually seeing it play out in its ability to therapeutically address various conditions that at its core is a dysregulation in how your brain functions and works.

And one of the major functions of this nutritional strategy or this particular diet is the reduction in carbohydrates that facilitate the cascade of events within the body that essentially shifts the whole body's metabolism away from a sugar and carbohydrate dependent form of metabolism towards a fat in ketone-producing form of metabolism, which has an array of different effects.

In fact, we've studied just the mere application of ketones independent of diet change and see profound effects in various conditions, including in extreme environments like high altitude hypoxia exposure for a special operations command grant looking at the ability to improve resilience against hypoxy exposure.

anywhere between 15 to 20,000 foot altitude, immediate exposure, and it increased the ability to have retained cognition in these extreme environments.

And so there's quite a fascinating array of effects that this diet or its metabolic constituents Uh, that are produced as a by-product of this diet can have on the body and its function.

Why insulin and carb-centric thinking took over

So it is at its core, a powerful, multifaceted, therapeutic approach was essentially a choice, I change in the choices you make when you walk into the grocery store.

All I can say is who knew, right? I mean, you know, what you're saying is you are getting back to a way of eating, of targeting our genome. as it were, the genome that's evolved over tens of thousands of years with the signaling that it is used to, that is expecting.

And the aberrancy of modern diet in terms of how it's interpreted by our genome, I think is the source of virtually all chronic disease. You're talking about neurodegenerative conditions.

So even Alzheimer's and Parkinson's with your friend, Tim Noakes, we recently published or wrote a book chapter

on the utility of ketogenic diet as it relates to Parkinson's while working with another team.

So the idea of powering neurons and importantly, I think, power microglial cells efficiently, in other words, targeting their metabolism, really sets the stage in my world for better brain health.

It's all about that. But why did this shift happen then? If for centuries then that this information was available, that look, when you cut carbs and sugar, things are going to do better early on.

Then with the advent of insulin, what happened? What happened to the food pyramid? Well, I know we know how the Food Pyramid evolved and how it recently changed.

We should talk about that. But how do people get into this mindset of, live your life however you choose, and we'll just cover you with insulin? That specifically happened right after 1921. This was when insulin was first discovered by Banting and Best and McLeod, who was also part of that discovery.

And I know this very intimately because I worked at a research institute called Samsung Diabetes Research Institute, and William Sansong would communicate letters, which I personally read that are still stored at the Institute to Bunting and best on how to take calf or cow butchered byproduct and ultimately isolate out insulin from that butcher by-product.

And then they gave the chemical formulation on how to isolate our insulin and then inject it. So William Sanson, where I used to work, was actually the first person in the United States of America to both chemically extract and also administer insulin to save the life of a patient in United And so I'm very, very intimate with the story because it was also after that discovery and after it won a Nobel Prize that William Sansom, the founder of the Institute I worked at, also published a paper in JAMA in 1925 where he then argued that patients with ability to administer insulin should now have enhanced freedom in their dietary choices.

He made this recommendation. in the absence of any serious rigorous randomized control trial evidence. It was simply a thought that this would improve the liberty of the patients on their diet because prior to 1921 it was standard of care utilizing a low carbohydrate approach even before insulin was even discovered extended the life of patients with diabetes.

This had been known for for over a century. But when insulin was discovered, the thought was, okay, now we have the tool that was absent. Now we can just administer this tool and eat whatever you want.

This became pervasive from 1920s onward. And most of the major medical research advancements weren't on nutrition, despite nutrition still today, 100 years later, still being the most important and impactful component of lifestyle on glucose and insulin levels, the two most important molecules and the management of diabetes.

But all this research would now go into advanced new insulin strategies, technologies, and now advanced curative therapies. All of that money has been poured into these other areas.

In fact, I've done an analysis between how much money or how has gone into research for things like therapeutic strategies and pharmaceuticals, technological advancements, just compared to diet-based innovation and publications.

And there are fourfold higher, more publications in just pharmacological and technological advancement than there is in nutrition. Despite nutrition having the most potent impact, every day on a person's glycemic control and insulin levels with diabetes.

Now that's why this shift happened at that time and the American Diabetes Association in 1970s for the first time came out with their first nutritional guidance and essentially what they did is they modeled the U. S.

dietary guidelines that first came Yeah, you know, I look things maybe are going in a better direction, but I think that, to me, it's always been a question of follow the money, right?

Even in my world, It's very frustrating that the narrative is live your life come what may, and suddenly when you're cognitively impaired will develop some wonder drug for you that will gobble up beta amyloid or whatever.

the theory du jour is, and hope for the best. But I think we're seeing a shift. And I, think the ball's getting hit across the court to our side of the net now, of, the Court, that we, we need to, uh, We need, to take agency and, you know, primarily, it's, nutrition.

Let me talk about, ask about what is this actually mean, ketosis. I know in your paper, You talk, about measuring beta-hydroxybutyrate levels and define ketoses as 0.5, I million moles per liter.

And how does that relate to the doctor who's skittish about a patient going into DKA or diabetic ketoacidosis? So we actually wrote guidelines for healthcare practitioners on how to interpret this and also administer this in the context of something like type 1 diabetes, where yes, even the subtle elevations of ketone bodies And someone with type 1 diabetes would immediately alert a physician or endocrinologist or healthcare practitioner that this patient's at risk for diabetic ketoacidosis for the sheer presence of ketones.

But endocranologist should know better than anyone because of the history of fasting was an endochronology assessment. or it was a tool that studied quite robustly in endocrinology that when you reduce carbohydrates in the diet through nutritional reduction while keeping calories high or through fasting, the ketone bodies are a natural byproduct of fat metabolism.

So when the body becomes more reliant on fat as a fuel, ketones are by default going to elevate as result of that. fats go through fatty acid oxidation, then the byproducts of those can go to ketogenesis.

That's just normal metabolism. But in the context of type 1 diabetes, the assumption is that all patients are going to be on these higher carbohydrate approaches and that this should have a sheer absence, especially with abundant insulin, of ketone production.

But yet, when individuals go on low carbohydrate diets, we know that a natural byproduct of that is ketone elevation. And so there's a key distinction here.

When someone's in diabetic ketoacidosis, there is high glucose levels, deficient or near complete absence of insulin, and unregulated ketones levels sometimes north of 10 millimolar per liter.

But in nutritional ketosis, in the context of diabetes or not, it is normal and regulated glucose levels, low but still present insulin.

Measuring ketosis and understanding ketone biology

So it's not an absence of insulin like in DKA. It's just a lower level of Insulin that keeps glucose and ketones in regulated levels. And ketone levels range anywhere I would actually change that barometer from 0.3 millimoles per liter upwards of a rough estimate around 5 milliliter, but we know that individuals can produce much higher than that on a fast, sometimes north of almost up to 10 milli molar on fast.

So it's really more so the focus on glucose and insulin because in DKA, those are both completely dysregulated in the context of but in nutritional ketosis, they're in normal ranges.

Hey everyone, we're gonna get right back to this podcast, but first I wanted to share some information about olive oil. You know that I love olive. So here's a good tip.

The most delicious olive that you can get is olive, oil that comes fresh from the farm. This is when the olive is at its peak flavor and all the nutritional good things that we talk about, the polyphenols, et cetera, are really at their peak.

When you buy your olive oil at the supermarket, you are getting an inferior product because they have been sitting on the shelf for months and they basically grow stale.

And that's why I've been getting my olive well direct from small award-winning family farms really around the world. Thanks to a fellow named TJ Robinson.

I have done Instagram live with him in the past. He's known as the olive-oil hunter. he's sort of the Indiana Jones of olive. He is able to source farm-fresh oils that are vibrant, they're healthful, their grassy, They're incredibly delicious.

And you can use them on whatever you want, on salads, fish, vegetables, meat, and even like I do on scrambled eggs. So if you wanna taste the difference that freshness makes, TJ is gonna send you a full-size bottle, which normally will cost you $39. He's gonna sent it to you for free if them just a dollar that will cover shipping.

And that's how he then is able to introduce all of you to this fresh pressed olive oil club, a club that we are members of. So there's no commitment, just send him a $1. He'll send you a full bottle of olive.

You just want to go to getfresh389.com. That's get fresh 389 dot com and he'll make it happen for you. Let's get right back to our podcast. So Andrew, let me ask you a practical question.

Not that these are not all practical, but I want to measure my ketone levels and see that I'm getting into ketosis. I am doing all the good things that you've talked about and other things we haven't talked yet.

What's the practical measurement? What can I do? Can I measure beta-hydroxybutyrate directly or are we looking at surrogate markers? So you can look at three different measurements of ketone production.

One is beta-hydroxybutyrate, which is the primary ketones body produced by the liver from fat metabolism. And you could test that just by pricking your finger and doing what they call a capillary measurement, a single blood stick with a meter.

The primary meters that people can utilize is either from… I actually prefer to use Keto-Mojo. They're a validated product and they're the most cost effective on the market.

There's also Abbott technologies, which is much more expensive. That's the one that's been around for ages. And that a way of just assessing at any particular moment.

So you wake up one morning, you're fasted, that you start to drink some water, your sufficiently hydrated and you test your ketone levels and your above 0.3 million molar.

And why do I say 0.3-millimolar, David? Because when you look at studies where people are on higher carbohydrate approaches, they're almost never above 0,3 millimolars.

So for me, 0.,5 was an arbitrary cutoff that had been used for years. 0,.3 is an actual measurement that illustrates you are higher than what someone would be if they were on a high carbohydrate approach.

So, I like to use 0.3 or higher as a measurement of actually being in ketosis because people like athletes or people with higher muscle mass or are people who are exercising regularly by default have lower levels and just not hitting an arbitrary cutoff of 0,5 doesn't mean they're not actually in Ketosis or producing sufficient ketone bodies.

But you would practically measure it with a blood meter like we talked about in the blood. There are other forms like acetoacetate which is really hard to measure without an advanced laboratory test or acetone where you breathe into one of these new technologies that tells you, you know, red, yellow, green as an indication of whether you're producing acetones.

But truly the gold standard is to do a capillary measurement if you want to practically assess whether your in-ketosis and shooting for 0.3 or higher as a measure of actually being ketosis is a good starting point.

The breath test for acetone, however, is talked about in social media quite a bit. What are you telling us about that?

So you can do it, but it's a byproduct of the ketone molecules that actually produce the most meaningful and well-known effects.

Acetone does have an effect, by the way. We've actually assessed this in some of our studies in seizure models where we administered exogenous ketones bodies and actually saw that acetones was profoundly higher.

And so, in and of itself, it's its own ketone level and is elevated on a ketogenic diet, but it is usually a secondary measure or indirect measure of what someone is really trying to understand, which is their beta-hydroxybutyrate levels, because that level, what you call BHB or beta hydroxy butyrates or blood ketones levels is the biomarker that's been attached with all the research we know about the health benefits, anti-inflammatory, antioxidant effects of ketone bodies themselves.

So that is typically the focus of what most people tend to look at and care about. So what happens then to the beta hydroxybutyrate that our bodies are producing?

Where does it go and how does that affect metabolism? So it can be used as a metabolite for energy. We've known that since the 1960s that it could actually be utilized for brain energy metabolism and it's utilized by the brain in a dose dependent manner, meaning The more that's present, the more your body is going to metabolize.

Many people would argue that illustrates that it's a preferred fuel for the brain, and I think that that is a sound argument. It will also be metabolized by other tissues like the muscle and various other tissue in the body, but it is more than just a metabolite for energy.

It's also a molecule that facilitates signaling. We know that it can actually change epigenetic signaling by changing acetylacin. There's actually something called beta-hydroxabutylation, which is an epi-genetic change for your audience who's probably a little aversion to this because they're listening to you.

But epigenetic changes means that the things went on the genome or your genes that regulate what genes are expressed or not expressed. So basically changing how your jeans are actually utilized.

That molecule does that reliably. And one of those genes is a FOXO gene, which specifically is an antioxidant producing gene. Which so as a way of actually causing anti or scavenging oxidative stress molecules.

And that's been looked at quite a bit. There's also an anti-inflammatory properties where it has been shown to directly even block certain, what they call, inflammasomes, NLRP3.

A inflamma zone is a great example. But we also know there's various studies, systematic reviews that have looked just at the ketogenic diet in general as a tool for reducing inflammation in individuals.

And that has been well characterized. So to your original question, these ketone metabolites are not just, are energetic substrates, but they're much more than that.

They change the way your genes are expressed. And they have antioxidant, anti-inflammatory effects and do quite a lot more that we've ever appreciated as well, because we have administered them in extreme environmental settings to look at their effects on cognition.

While they are improving cognition, David, in these extreme environments like high altitude hypoxia exposure, We also see that it increases the amount of oxygen the body uptakes as well, and also potentially changes how the buddy regulates oxygen with chronic administration, which is a novel area that we're about to publish on here shortly.

So when you sit with administration, in other words, exogenously administered beta hydroxybutyrate? Correct, yes. And there's multiple forms on the market that have diverse potential application and their utility.

For example, we did a Department of Defense Special Operations Command grant. The product we used was from

a company known as HCMN, but called Ketone IQ.

This is a 1,3-butane-diol-based product, which is converted in the liver. So when you consume it, it goes to the livers, converts to ketone bodies. Your body will then utilize those ketones bodies for various uses.

One of the effects of 1-3 butane diol based products, because it's not the only one, there's other ones that attach other ketome molecules to it. is that you have a slight change in the hydrogen ion levels within the blood and that subtle elevation hydrogen ions in blood seems to change the ability to uptake oxygen levels through ventilation.

And it kind of works like how we anticipate it works, like Diamox does. Diamux is a mountain sickness drug. that specifically causes mild metabolic acidosis and increases SBO2 levels for people to attenuate mountain sickness when you get to low oxygen levels.

Exogenous ketones, MCTs, and performance applications

Well, ketone bodies do the same exact thing without the negative side effects of Diamox, which reduce cognition and physical performance. So there's an array of effects ranging from the genes to signaling to just pure metabolic effects, and some of which are just now being discovered.

So interesting. So it sort of emulates a carbonic anhydrous inhibitor. Yes. A carbonous an hydrous inhibiter. What that is doing is actually causing a blocking specific processes within the blood to elevate hydrogen ion, subtly reduce the pH causing on a mild metabolic acidosis.

That mild, metabolic acidosis is the same as that. the mechanism by which oxygen is allowed to be brought into the body at higher levels. And we know the ketones do the same thing, but you can actually pulse it at periodic intervals up to your volition.

Diamox is something that works over hours and hours, and it's a prolonged drug for obvious reasons. But there might be a setting where you want to just therapeutically administer something for an acute period of time.

and see potential benefits from that. What's distinct, though, about ketone bodies versus drugs like Diamox, which is why I think just the theme that I have observed over the last 20 years of being in research is that the more we get back to natural processes within the body, the better off we tend to be, And what am I saying here?

I'm saying, okay, when you use something like Diamox, it lasts for multiple hours, but we also know it reliably reduces cognitive performance, reliably it reduces physical performance.

But what we are observing is that when we apply exogenous ketones into the same extreme levels of hypoxia, we're pushing people to 20,000 feet. So we aren't quite at Everest but not far off of it.

And even in those extreme settings, we were seeing that we increased SBO2, increased resilience against cognitive decline, and actually improved cognitive function against a placebo-controlled arm.

So illustrating that these molecules have clear effects in diverse settings and change physiology quite profoundly. Hey, we're gonna get right back to the podcast, but I do have an important message.

You know, for decades we've been told that our genes are basically our destiny as it relates to health and that everything's locked in place predicting even our future brain health.

But let's be clear, your DNA isn't a verdict, it's a roadmap. And I'm talking to you today about 3X4 genetics. I actually described them in the new book, Brain Defenders.

And this is a company that helps you understand your genetics, what you've inherited, and I think more importantly, how your daily choices can influence how those genes are actually expressed.

In other words, you can control your own genetic expression. And you know, that matters for your health and it really matters to brain health, including things like memory and mood and cognitive resilience.

You may carry genetic markers associated with cognitive decline, like as we've talked about APOE4, But possession doesn't equal expression. Your lifestyle, your nutrition and metabolic health, all the things that we talked about here on the podcast.

can powerfully influence which genes are turned on and which stay quiet. The 3×4 Genetics Test looks at how your genes impact brain function at a cellular level and, which then, through the 3X4 Health Journey, in which they provide you, guides you through a clear and a science-backed program focused on inflammation, methylation, oxidation, oxidative stress, things that we routinely discuss here on the podcast that are the key drivers of basically what makes a good brain go bad.

And we have spoken with the team at 3X4 Genetics and they were able to get a special offer for our podcast community. So head on over to 3x4genetics.com forward slash drpearlmutter and get that special and start really your personalized brain health journey today.

Let's get your genes working for you and let's go back to the podcast. And I would suspect that this then is synergistic along with hypoxia-inducible factor 1-alpha, one would think.

So I don't know because we didn't actually test biomarkers in our analysis specifically for HIF 1 alpha, but there is some potential looking at that actually in cancer settings.

as someone who used to look at the ketogenic diet and actually hyperbaric oxygen therapy as a tool to regulate HIF-1 alpha and because of that being a key regulatory molecule in the context of cancer due to hypoxia based signaling.

I'm digressing a little bit here, because in this specific setting, we don't actually know. I shouldn't do that, but my mind's going there. But anyhow, let's get more practical.

What is MCT oil, which is over the counter, and people buy it and use it? How does that play into the idea of amping up the production of things like beta-hydroxybutyrate, not actually a ketone, other ketones?

So this is a great way of kind of segueing to what are the array of various ketones that are out there. MCTs or medium-chain triglycerides are in things like butter, coconut oil, breast milk.

We know that that molecule when ingested They're called C8 and, uh, C6, there's also C10, but C-8 probably being the one that converts most readily to ketone bodies in the liver.

When they're ingested, they are consumed, shifted, absorbed through, um, an MCT transporter, the same transporters for lactate. It goes into the body.

Once it gets to the, liver, to liver will rapidly convert medium trained triglycerides to, ketones bodies. These ketons bodies, obviously then elevate circulating, a keton levels.

which there have been studies actually showing that MCT-based diets or natural forms of fat that convert to ketone bodies and epilepsy have also been shown to work almost as effectively as just ketogenic diets do in and of themselves.

But what's interesting about MCTs is they were the first, quote unquote, exogenous ketones that had actually been studied for therapeutic use back in the 1950s and 60s.

for malnutrition disorders in children. So kids that were undernourished or not able to grow sufficiently, they were actually given MCTs. The theory was that this was a way of overcoming some of the malnutrition issues that some these children had in the gut.

And it effectively worked. It increased body weight in these kids. But it was actually the first time therapeutically that ketones were ever administered outside the body and elevated ketone bodies.

Because they did in fact prove that in multiple analysis after those studies were conducted. But there was an advent of an emergent forms of various other ketone bodies.

So then in 1962, MIT actually studied 1,3-butanediol, which is in products like keton IQ, for aerospace transport. Why were they interested in that? Because it was a very shelf stable molecule.

that could go into outer space with high caloric density. So if you have a carbohydrate, for every gram you're only getting 4kcals. But things like MCTs, which is a fat, you can get north of almost double the caloric density, but if it can…

If you could have things, like 1-3-B-10-dial, that also have higher calore density and you consume them, it wasn't so much they were focused on ketone production at the time, they're actually worried about shelf stable nutrients in outer-space.

And that was where that first looked into. But there was an emergence of various other forms of ketone bodies that have since come out over time that had looked at ketones salts, ketonesters, and will continue to see emergence in various forms, including free acids or combinations therein for various therapeutic applications.

And I'm excited to this because I've studied novel formulations of keto bodies for the last 20 years and I can tell you that there's a tool, a time and a place for many of these.

But to be fair, it's not as if you can take a couple tablespoons of MCT oil and then not pay attention to what you're eating. That's absolutely correct.

It is not an eraser for bad life choices. These are simply tools that can be incorporated. I like that. Yeah. He doesn't erase your bad choices and lifestyle habits that you have.

What it does do is it can add to a comprehensive nutritional and life style strategy that is positively affecting someone's health outcomes. But no, in and of itself it's not going to just erase someone health problems, nor does virtually anything really.

Very few things are simply a magic tool in the toolbox that fix all problems. Some people would contend that GLP-1 receptor agonists are creeping up on becoming something like that, but even those aren't without their problems.

We know that they have GI issues. You have to be conscious of muscle mass with these byproducts because of how rapidly the weight loss issues arise. Either way, we can go on and on.

There's nothing that's for free in life, right? No, I'm not sure I would agree with that. I think exercise is for You got to buy a pair of what we used to call sneakers, but it's pretty much that what's the downside, you know, anyhow, we're, I want to cover something and I promised in our, in the introduction your, your paper that you put out, uh, In just last month carbohydrate ingestion on exercise metabolism and physical performance and you know my take away from this is four years we've been told for for example and endurance event you are back in the day when i was long distance runner.

had to carb load the night before. And in fact, there were always the pasta dinners that were part of the experience and all that. I think that you really kind of turn that upside down.

Carbohydrates, endurance exercise, and the new study

The whole notion of needing carbohydrates for exercise, athletic performance, you very much have challenged. First, how again did we get into this mindset of we've got to burn carbs when we exercise?

And then let's unpack your new study. Sure. So that has a very similar story arc to some of the things that we've seen in diabetes where in the 1960s, so let's look at Olympic games.

Olympic Games are a great way of assessing what were the best athletes at the time consuming. Well, we knew prior to the 60s and 1970s that the Olympians were predominantly catered and were consuming foods that were protein and fat focused.

Doesn't mean there were zero carbohydrates, but it was a priority around protein, a It was until the 1960s where a physician named Jonas Bergstrom discovered the ability to actually stick a syringe into the muscle and do something called a muscle biopsy.

So they called it the Bergström Muscle Biopsi, where they actually suction out a piece of muscle. And what they were finding is, oh wow, lo and behold, when we pull up muscle, and analyze that muscle tissue, glucose was being stored as something called glycogen.

So glucose molecules bound together in these chains. And so the thinking was, well, if they're stored in the muscle, they must be essential to physical function and performance.

They had actually run studies that had showed, oh, look, when you consume more carbohydrates, not only do you have more muscle glycation stored and those muscle tissues, but you also perform for longer.

It was actually 10 years later when they discovered a new technique, the ability to consume oxygen and exhaled carbon dioxide, the ratio of those two molecules were actually a measure of how many carbohydrates and fat someone was burning.

And at that time, what they discovered yet again is that when you consume more carbohydrates, no surprise, you burn more carbs. But there was an association yet, again, for performance.

Now, keep in mind, David, these are just associations. These are not causal experiments to prove that muscle glycogen. Right. It does not mean it's not causality, but let's keep going.

Yes, true. So it doesn't prove it's causal, but it does not disprove it is causal either. Absolutely correct. It was in the 1980s and 1990s that they were discovering, oh look, when athletes perform at higher and higher intensities, that there becoming more reliant or almost obligate requirements for carbohydrates because if you get too high in intensity, you shift over to more of an anaerobic based metabolism and you must quote unquote need carbohydrates.

Okay. Well, in the 2017 to 2021, prominent researchers do really, really rigorous research, studied low carbohydrate intake, Luis Burke, John Holly, and a few others, where they lowered carbohydrates in elite race walkers for five days to three weeks.

That timeline is very, very important here, David. But they did it for a short duration form on the diet where the athletes were still transitioning on a diet.

And what they found is that while the athlete were transitioning into ketosis, they were already producing ketone bodies but not fully transitioning by all measures, at least not confirmed.

They saw a deterioration in performance, but only 2%. So most athletes would never even care about 2%, but if you're an Olympic athlete, that's the difference between first and second place.

So this got a lot of press. This really was what the title of the article is, Nail in the Coffin. for low carbohydrate intake as a nutritional strategy.

But what was interesting about all these analysis all along was one, it was an association analysis between these biomarkers of glycogen or carb loading to increase glycation levels, which is what you were talking about with

pasta, right?

The idea that we load the muscles up or card load to increased glycagen levels or this other measure of carboxidation. Now, these studies in 2017 to 2021, one of the big issues around them is that their duration on the diet.

We have known since the 1960s, David, from George Cahill, that when individuals go on to these very low carbohydrate approaches, in the most extreme rapid form of that is a fast, that even we don't see a normalization of key brain energy metabolites until around after three weeks in duration.

But all these studies were looking at ketogenic diet transitions less than three-weeks or less. And so what we decided to do, we said, wow, this is really interesting.

We know that a lot of athletes may consider doing these low carbohydrate ketogenetic diets for all the therapeutic reasons we've talked about. But they're often talking about how they are concerned around their performance.

But no one had ever really done a rigorous randomized control trial for four weeks or longer in duration where they controlled the calories, the body weight, and the activity and did a control for genetics and environment by doing a crossover design.

So we did it multiple times. We've run multiple analysis looking at athletes who were high level athletes, fit, high VO2 max athletes. Who were competing in regional events.

Actually, we had a study with Ironman competitors and what we were assessing was if we put these athletes in control, all of these confounding variables that prior studies had not, which impact performance What happens when we study that and control for those variables for, let's say, a 6 by 800 meter sprint, an intensity level over 85% of the athletes VO2 max, when carbohydrates would be virtually all the energetic metabolic substrates for that activity, at least hypothetically speaking.

But what we found is that when athletes were either on a ketogenic diet or on high carb diet doing six by eight hundred meter sprints or a max effort one mile time trial.

So the fastest you can run for four to six minutes in duration. We found that the ketogenic diet did not produce any deterioration in physical performance in these high intense athletic endeavors.

And when we looked at what was fueling these athletes up to over 85% of their VO2 max, fat metabolism made up the majority of fuel substrate during this activity and There was a level of fat oxidation that was higher than any fat levels ever reported in the medical literature.

Some athletes were over 1.85 grams of fats burned per minute during physical activity. But gram for gram, that's almost twice as many calories as they were going to get from burning their glycogen or glucose.

Correct, and why is that important? It's essentially important because what it told us was that the belief that when you get to these very high intensities that you were requiring carbohydrates was not in fact true.

It is dependent on the nutritional context. And what we were finding is athletes who are more fat adapted for at least four weeks or more in duration, that they were able to tap in and sustain physical activity with fat being the predominant form of fuel, even north of 85% of their VO2 max.

that challenge. Let me stop right there because what you just mentioned, I think many people will understand the notion of metabolic flexibility, the ability then to tap into fat and that doesn't come quickly.

You say that what was flawed in the earlier studies is they looked at people early on, they didn't draw their studies out long enough to allow the subjects to enter the physiology of metabolic flexibility and have that opportunity.

Unpack that a little bit for us, because I think it's really important for people who want to shift a bit and become more adaptable in terms of a higher fat diet, less carbohydrate.

Sure. So what these researchers did who are looking at shorter duration diets from five days to three weeks is they were specifically focused on ketone levels and fat oxidation levels.

That was the primary thing they're focused. And that's obviously very important. Those are both clear signs that athletes or any individual is shifting towards a ketogenic metabolism.

But what was not focused something that we focused in on a subsequent study was key brain energy metabolites. Like glucose and ketone levels because we know that and we'll talk about this in a minute in our recent review That these metabolites since for over a hundred years have been shown to be related and impact Mechanistically induce early onset fatigue.

So we that blow blood glucose levels in the blood Induced glycopenia in brain and could reliably induce earlier onset Deteriorations of physical performance and induce profound fatigue we've known this for 100 years, but These researchers were not really focusing on whether these individuals were seeing normalization of glucose.

What we did in our subsequent study, after that initial short duration high intensity effort, was we looked at, okay, what about if you do the extreme opposite of that?

We're going to get athletes who are doing Ironman competitive events, which means they're swimming, cycling and running for huge durations of time at high intensities sustained.

And so what we did is we asked Ironman competitors to come in. What we wanted them to do was sustain 70% of their VO2 max on a cycle bike for as long as they could before they fatigued below the 70 percent threshold.

Or it got something like essentially reduced induced fatigue. What we were finding is that when we compared the same athlete for six weeks on both of these diets, and we went beyond the four-week mark to six- weeks to ensure they were adapted on this diet, we found that yet again, athletes on the ketogenic diet did not see a deterioration in performance.

But what was absolutely critical to this, David, is the athletes in the keto diet actually had a higher incidence of hypoglycemia. Yet they maintain the equivalent level of physical performance.

How did they do that? Well, when you actually calculate the amount of brain energy metabolites circulating in the blood, not just glucose, but also ketones and lactate, all fuels for the brain.

The high carbohydrate athletes and the ketogenic athletes had the same amount a brain, energy, metabolite circulating and blood. Yeah, I think we have to, in this situation, moving forward, redefine then what does hypoglycemia mean, because that sounds pathological.

But I thing it's hypoglycemias based on previously standardized lab measurements. Correct, how do we define hypglycemia as it relates to somebody who's fully keto-adapted?

This is a great question because in the medical literature, 70 milligrams per deciliter, 3.9 millimolar is used as the threshold for hypoglycemia. Why is it used a threshold of hypoglycemias?

Because the vast majority of people will experience symptoms at or below that level. But if you actually look at the literature on this and these clinical physiology studies that have been going on for 40 years, there are people who experience hypglycemia when they go below 80 milligrams.

And the rate at which their blood sugar is dropping is also an issue. And I can tell you personally through lived experience with type 1 diabetes that the rate of change in glucose has a clear neurological impact.

You can feel the physiologic difference from a change of glucose levels that is fast and profound. It is a very clear and obvious effect on the body. There's actually some emergent research, although I don't know if it's published yet, so I cannot speak too much to it and just say that there is some interesting data showing that change and glucose does relate to cognitive function.

That's right. I'm aware of what you're talking about. Yeah. So what we were finding here, David, was that athletes who are doing very low carbohydrate ketogenic diets versus high carbohydrate diets were seeing no significant differences in performance between these two dietary shadows yet again.

What was interesting is that when we equated for total brain energy metabolism, they were the same. Yet, despite one diet having dramatically lower carboxidation levels and dramatically low glycogen levels.

This directly challenged the belief that glycation and carbohydrate oxidation levels were pertinent or essential to performance. One other thing we did in this study as well is we also administered a strategic amount of carbohydrates.

Just enough carbohydrates David to prevent hypoglycemia, but not enough Carbohydrates to change glycogen levels or carbohydrate oxidation levels. Why is that so important?

It's essential because what we were trying to do is understand if we just gave enough carbohydrate to normalize blood glucose levels, which was 3.3 grams every 20 minutes.

So every hour we were giving 10 grams over the hour during these prolonged strenuous forms of exercise intensity in Ironman competitors. This is six to nine times lower than current standard of care or current sports nutrition guideline recommendations for fueling for athletes.

We were only trying to control blood glucose levels. Well, when we gave 10 g per hour on both the high carb diet and low carbohydrate ketogenic diet both diets improved performance 22%. So it showed that yes ketogenetic diet athletes can bonk and so can high carbohydrate athletes but if you normalize blood glucose levels in both of these or increase the amount of brain energy metabolite circulating the blood that this improved the performance dramatically.

Now, one thing here, David, is that we did a major review that was published in Indocrine Reviews where we looked at over 100 years of evidence, over 600 studies, and over 160 different sports nutrition studies or sports performance studies in the context of carbohydrate administration.

And what we found is when we look at these 160 studies when carbohydrates reliably improve performance, What was happening is that the placebo group of those studies, 88% of the time, the placebo or control group was seeing a precipitous drop in blood glucose levels.

So it wasn't so much what was happened in the carbohydrate treatment group.

Fat adaptation, glycogen, and exercise fuel use

It was this precipitous drop in blood glucose in the control group that was seeing 88% of the time across 160 different sports nutrition studies when carbohydrates improve performance, the most reliable bottom line.

The reality is, though, it's not as if your body is going to be in a situation of flex fuel. Well, if I'm low in carbs, then I can just shift over and burn fat.

There are actual mechanisms involved. in when you consume a higher carbohydrate diet that actually exclude you from being able to beta oxidize. So how does that work?

How do we shut off fat metabolism when we're consuming higher carbs? Yes, people lose their mind when I bring this up, but it's just the hard facts when When you consume higher carbohydrate intake, David, what we see is that

higher carbohydrates intake increases blood glucose levels.

What happens when you increase blood-glucose levels? The pancreas releases insulin instantly into the bloodstream. That insulin will go to the fat tissue and reliably prevent fat breakdown.

If you prevent that breakdown, you're preventing one of the most important fuels on the body from being utilized during that exercise. So what happens during exercise for athletes who have high carbohydrate load, high glucose load and high insulin load?

They reliably expedite the breakdown of muscle glycogen. Why? Because you're shutting down the other forms of fuel. In fact, there's a key figure in our analysis and endocrine review.

It's open access. Anyone can look at it. Its figure 19. What you'll see is that when they compare 120 grams of carbohydrates per hour compared to just 25 grams per One, at 120 grams per hour, insulin was infinitely higher, but you essentially blocked fat metabolism to around 10% of total energy substrate used during a prolonged, strenuous form of exercise.

and you expedited muscle glycogen breakdown. Over 85% of the fuel came from glucose, and most of it from muscle-glycogene. But when you were looking at the much lower levels of carbohydrate intake with much low levels insulin, fat became a profound form of energy substrate during the exercise, making up over 50% energy requirements during exercise.

And guess what? The output during exercise was equivalent. It was the same. So what happens when they consume more carbohydrates is you're essentially shifting around where the body is getting its fuel.

And what we were finding in our study is just giving 10 grams per hour was sufficient to normalize brain energy metabolism. Again, focusing on this key tissue of the brain actually impacting performance, just 10 grams per hour, normalized blood glucose levels, normalize brain energy metabolism, and increase performance on both ketogenic athletes and high-carb athletes 22% during this study.

Andrew, let me ask you, for an endurance athlete, in terms of energy resource, energy depot, how does our body fat compare to our glycogen source in term of providing us a resource for energy?

Glycogen levels are very finite, very limited. So the average body weight male can probably hold somewhere between 500 grams of carbohydrates, so 2,000 calories in the form of muscle glycogene.

Females around 300 or so, obviously a little bit more than that if you're well trained. That's around 500 grams or 2,000 kcal. If you look at some of these athletes who are doing profound, prolonged, strenuous forms of exercise, they're burning through huge amounts of calories over time.

Take Tour de France as an example. They'll go four to seven hours for back-to-back days, almost up to a month. There's huge amount of caloric burn, but you only have a finite amount resources and up around five hundred plus ish grams for an average body weight male.

to store glucose and finite resources within the muscle. However, you haven't have fat to typically last on a fast for months, even for lean individuals.

There's examples of individuals north of 400 pounds that have fasted for over a year. So fat is a resource of clear abundance, and the body mechanistically set it up that way so that you can easily store fat, so you could easily tap into this abundant resource during feast or famine.

It makes total sense. And the way we know this is how the bodies prioritizes where insulin goes. When you consume food, particularly carbohydrates, David, as you know, many abolitionists will probably appreciate this for the first time, the place that insulin to the liver.

It goes to the hepatic portal vein, those insulin granules immediately released into the hepatocortal vein. Why is that important? It's goes through the liver first, David.

It go to liver, first because the body wants to re-synthesize liver glycogen to maintain circulating blood glucose levels, to maintained brain energy metabolism.

Its only after it goes liver to make sure you have sufficient glycogen to maintaining blood glycos and brain metabolism that it then goes the periphery, the fat, the muscle.

Now there's key distinctions between the fat and the muscles. The fat binds insulin at very high potency, meaning you need very little amounts of insulin, at the fat, to actually shut down fat metabolism.

Not completely, but largely. You dramatically want fat breakdown with just subtle amounts insulin. This makes sense because the body wants to store its key long-term fuel that is required to sustain life over long durations of a famine.

Only after all of that, David, does it then go to the muscle and fills up, in the context of abundance, muscle glycogen. Only, after those priorities are addressed, then it goes and fill up muscle-glycogene levels.

As a result, you can start to fill this peripheral fuel. What's fascinating is when you actually look at the physical performance literature, And we go back to these studies in the 1960s, 1970s and 1980s that have focused on muscle glycogen being essential to performance, showing that the level of carbs being burned is essential for performance.

What you also see in these pivotal studies that change the way we focused carbohydrates, because if you focus on the muscle-glycogene, David, you would need to eat a huge amount of carbohydrates to refill it.

Well, when you look at those same studies, David, they showed a reduction in glycogen with associated reduction of performance. But in that same study, it also showed the group that reduced the muscle glycation also had profound reductions of blood glucose levels.

The authors failed to focus on blood-glucose levels, but they instead focused on glycan and carbohydrate oxidation levels despite us knowing since the 1920s that low blood glycos levels from Harvard physicians in JAMA in 1924 and 1925 Gordon and Levin, you can look this up in JAMA, have shown that low blood glucose cause glycopenia and early onset fatigue.

So despite in their own research they were showing low glucose levels, they focused on muscle glycogen and carbohydrate oxidation levels as the key associated predictors of performance.

But they never causally proved it, but sports nutrition guidelines largely focus on carbohydrate and substrate oxidation level as a focus of nutrition.

I can remember mile 11 or mile 12 in a marathon that everybody was busting out the gels and the sports drinks. By about 11 miles, everybody I think had gone through their glycogen.

I'm just in my mind thinking, where else do you think? What's going on in them physiologically? They hadn't adapted. And here you have this incredible energy resource that will take effort to shift over to developing the hardware, I guess, and software to be able to utilize it.

But Andrew, this is incredible information. I think it's really very important. It's going to really set people straight on what they think they need to do, especially as we talked about earlier, as it relates to type 1 diabetes and overall metabolism as that relates a chronic degenerative disease, but also here in the athletic performance world that, you know, I think there's still lots of work to be done, not from your perspective, but from the perspective of getting the word out that the science is there now, pay attention to it and let's start utilizing body fat, which is really what everybody wants.

But now of course we're challenged with the easy way out which are the GLP-1. So, it does kind of take us off the trail a little bit as it were. Well, there's many tools in the toolbox, right, that people can go out and explore and utilize.

What we talked about a lot here today is just the ability to tap into kind of one of the forms of our physiology that very rarely ever gets tapped into, this ability, to utilize fat as a fuel substrate.

And it has profound therapeutic potential in a number of settings. But what we've also… And this is a survival mechanism. that's deeply ingrained in who we are, that has allowed humans to survive for as long as we walk the planet.

This notion of shifting metabolism over during starvation, but also interestingly, we have mechanisms such that when we do consume sugar in the form of fructose, something very similar happens in terms of locking up our fat and reducing energy expenditures, reducing mitochondrial activity such that we can build body fat and maintain bodyfat.

And, you know, certainly not what we want to do now, but that's the mechanism of increased uric acid. So it's interesting to think about everything we've talked about today through the lens of these being really powerful survival and adaptive mechanisms.

I completely agree, but I would also say that there are many individuals, and I'm an example of one, who sustain these approaches for decades on end and have been able to do so while sustaining high levels of cardiovascular health and bone health, liver kidney, thyroid health along the way.

And so when people often think about it as a survival mechanism, they don't always appreciate, the kind of view it has the extreme. When in reality, what one could contend that our current food environment is the extremely, it is an extreme form of constant food exposure to low nutrient available food options.

That are the most likely to be over consumed in an abundance in the, most accessible leading people to have an array of chronic health issues. In fact, a major analysis from 34 different countries from Duke and other investigative researchers all over the world, including China actually showed that 90% of the obesity epidemic could be explained.

By diet alone and the remaining 10% wasn't necessarily a lack of physical activity, but just alterations across individuals and energy.

Food policy, metabolic health, and closing reflections

You can exercise away a crappy diet. It's been said before, But having said that in closing, I would suspect that you're feeling somewhat positive about the new USDA food guideline recommendation that was just published.

I think it's a great illustration of understanding where we are as a nation, which is that nine out of ten individuals have suboptimal metabolic health as defined by a fasting blood glucose level that's elevated high triglycerides, elevated waistline or some other metabolic biomarker.

The nine ounce of Americans are clearly showing adverse metabolic changes in those biomarkers. And the fact that 90% of American is a sub chronic or chronic metabolic health issues that we need to address that with the nutritional strategy that directly addresses those chronic issues.

Otherwise we're only addressing food guidelines for 10% or the population. So I think that what has been done in the United States. of America where they're focusing on specifically reducing sugar and sugar alternatives that are hidden on food labels.

The increase in protein intake, which is a really incredible nutrient that reduces, helps reduce hunger more so than carbohydrates and fat do and are great for supporting muscle function.

And also doing a number of other key things. that have not been done before, a lot of people who are pushing against these dietary guidelines say, oh, well, this is not that different.

No, it's very different, for example, when they said 10% or less of the calories come from sugar, what people don't realize is that when people use a percentage in dietary guidance, and means that food subsidized programs in school lunches, snaps, WIC, other programs, could use any form and quantity of sugar in those programs because it was a percentage.

Because David, me and you may need way different caloric ranges. So percentage allowed for the individuals making up these diets to have total autonomy in how much they put in there.

What they did differently as a singular example, and they do this throughout the document and people don't realize this, is they on things like sugar.

Why is that important? It prevents these programs from overfilling forms of food subsidized programs which make up a huge portion of the American diet from things likes sugar, it prevents that essentially from happening.

So are these food guidelines different? Yes, they are. Are they better? I would argue they're the most functionally applicable to what actually will affect the American people.

Whereas people say, oh, look, it's the amount of wheat and grain and all these other things. They don't make up a composition that makes sense. What they aren't paying attention to is policy.

Yeah. I think back to 2021 when the last guidelines came out. And we, I wrote an op-ed in med page today with actually Dr. Casey Means, who's now before the Senate as we speak, getting vetted for Surgeon General, but nonetheless, and we challenged this whole notion of 10% of calories coming from sugar as being the recommendation.

And, you know, there was no science supportive of that then, nor is there now. So, that's a big issue. I think ultra-processed food, also a biggest issue, a study came out, evaluation of Framingham Heart Study data in the Journal of Prevention of Alzheimer's.

What a journal can you imagine prevention of Alzheimer's indicating that over the six year period, averaging one serving a day, just one, serving, a, day of ultra processed foods based upon what you and I've been talking about was associated 13% increased risk of developing Alzheimer during that six-year period.

a disease for which we have no meaningful treatment. Having 10 or more servings of ultra processed foods a day, it seems like a lot. You know, as well as I do, that's not uncommon when you add in the soft drinks, the flavored yogurt, you name it, was associated with a 2.7 fold increased risk of developing Alzheimer's.

That's 270% for those individuals comparing it. Yeah, affecting six million Americans currently. So anyway, Andrew, you are the man and you're an incredible researcher, but also I think importantly, such a great example for all of us.

You took the lemons and made the lemonade and it's just really great to talk to you because you walk in the talk and I so appreciate that you spent so much time with us today.

It's been an honor, David. I appreciate it and appreciate those who listened. We'll talk soon. Bye for now. What I appreciate most about my conversation today with Dr.

Kutnick is that it brings back the notion of nuance into a very polarized space. You know, the space between needing carbs for athletic performance, needing carbs if you're on insulin, and the idea of being on a ketogenic program.

Nutrition science has too often devolved into camps. The high carb camp versus the low carb. a camp rather than focusing on what is the physiology, what are the measurements that Dr.

Kutnick talked about today that we see in people on those specific programs. What he reminds us is that this notion of metabolic flexibility i.e. the capacity to efficiently use both fat and glucose, may be the real objective.

That's our goal, not to succumb to dogma or a particular ideology, but the idea of adaptability. And that really speaks to our heritage over tens of thousands of years.

Whether you're an athlete, a clinician, or simply someone interested in preserving brain and metabolic health, this is a discussion that underscores a powerful truth.

that the way we fuel our bodies shapes how our mitochondria work. And as I've talked to you extensively on this program, that is really key to our entire physiology functioning appropriately, how are hormones are balanced?

What is the level of inflammatory tone in the human body? And ultimately, what is our level resilience? If you found this conversation valuable, I know I did, Please share it.

These are the kinds of discussions that move science forward. So thanks again for joining us. I'm Dr. David Promutter here on the Empowering Neurologist.

Until next time, stay curious and stay empowered. Bye for now.