Understanding Nutritional Individuality for a Personalized Approach to Wellness
A Special Interview With Chris Masterjohn, Ph.D.
By Dr. Joseph Mercola

Dr. Joseph Mercola:

Welcome, everyone. Dr. Mercola, helping you take control of your health. And today, we're joined by Chris Masterjohn. Many of you know his work with Weston Price, which far preceded his getting a Ph.D. in Nutritional Biochemistry. And he likes all things nutrition, and likes to cogitate on that and explore the realm. So, we're going to have some fun today. So, welcome and thank you for joining us, Chris.

Chris Masterjohn, Ph.D.:

Thank you for having me, Dr. Mercola. It's great to be here.

Dr. Joseph Mercola:

All right. So, we had a phone conversation not too long ago, and we discussed coming on. And I don't really recall. We had some theories, I think, he wanted to explain, which we can start. So, why don't we – Do you recall that conversation?

Chris Masterjohn, Ph.D.:

Yeah, well, my big thing that I'm very immersed in now is understanding how we all are different. So, I think we-

Dr. Joseph Mercola:

Oh, that's right, nutritional individuality. I remember now. [inaudible 00:01:03] of Roger Williams.

Chris Masterjohn, Ph.D.:

Yeah. So, Roger Williams should be the father of this field, documenting many ways in which the biochemistry of different people resulted in different nutritional needs. For example, one thing that he probably would've recognized about me is that my eyes are light blue. I've got greater UV destruction of retinol inside the eye. And so, I'm likely to require a higher amount of vitamin A. And I think there were many people in between then and now who have tried to come up with ways to determine should you eat high carbs, should you eat low-carb, and all these different things. But I think we are now entering the realm where we can get a lot more precision on the hundreds of ways, really thousands of ways, that we are different.

And I think there are a lot of nuances that we are just now being able to come to, where it really takes a lot of work to get incredible precision. But we can now start thinking about things that

people can self-experiment with at home, such as how different metabolic pathways might be altered and why you might need to get most of your nutrients at just levels that might occur in a whole food, but maybe one particular person needs a lot of extra riboflavin, and another person needs a lot of extra thiamine. And if either one of those people do the opposite, they're going to wind up in a lot of trouble. And so, I think where we are now is really at the place where we want to start getting deeper into the precision that's becoming available.

Dr. Joseph Mercola:

And what is the technology that allows that precision?

Chris Masterjohn, Ph.D.:

So, in the modern day, I think what we have now is the development of the ability to look at this issue with a lot of precision that we did not have in past eras of trying to individualize people's diets. One of the major advances that we've had over the last year is that, as whole genome sequencing has become affordable to apply at mass scale, we now have studies. For example, the million-exome study, which actually didn't use the full technology of whole genome sequencing, but looked at whole exome sequencing, which is an approximation of that. And what it found is that essentially, genetic mutations are skewed such that any given one that you would think would be too rare to care about, the average person has one or two. And I think that's an underestimate, I think it's really three to five.

And what that winds up doing is creating a situation where instead of five years ago, when you would think nutrigenomics is understanding whether I have MTHFR (methylenetetrahydrofolate reductase), or I have COMT (catechol-O-methyltransferase), or I have one of these other polymorphisms that are common, where you can take a report and you can share it with 20 other people at a conference, or you're friends with and three of you will be like, “Oh, I have that one.” And the other six will be like, “Oh, I have that one.” We really have a skew where the highest impact genes are so rare that you are likely to go to a conference and talk about yours with someone else, and not run into someone that has the same that you have. And what that means is, a lot of times the most impactful mutations that someone has are – first of all, you've got 14 million, you can throw most out because they are so little in their impact that they're just noise, and if you boil it down to-

Dr. Joseph Mercola:

14 million what? The mutations? Or not genes?

Chris Masterjohn, Ph.D.:

Sites of variation.

Dr. Joseph Mercola:

Okay.

Chris Masterjohn, Ph.D.:

So, in the human genome there's 14 million sites of variation. And if you look at something like 23andMe, they are looking at hundreds of thousands of those 14 million. So, they're missing most of the sites of variation.

Dr. Joseph Mercola:

23andMe is not a human genome though, it's just a partial sequence, right? They don't do the whole genome-

Chris Masterjohn, Ph.D.:

What it is is a snip chip test. And so, what they do is they have a chip that represents each polymorphism that they're looking for, and they want to ask the question for each one, "Are you this one or that one?"

Dr. Joseph Mercola:

And just for those who don't know, a snip is a single nucleotide polymorphism, or a mutation, so to speak.

Chris Masterjohn, Ph.D.:

Right. So, before whole genome sequencing became affordable at mass scale, the most recent iteration of what people were doing to try to understand their DNA was doing something like 23andMe, or Ancestry, and then often running those through third-party reports. And those are extremely limited in what they're testing because they're only capturing a couple hundred thousand out of the millions of variations. But way more importantly than that, the nature of the snip chip test, the methodology that they're using, loses all of its accuracy when you're looking for something that is present in fewer than 1 in 1,000 people. So, the way that the test is done is it's dependent on the stats that you get from large numbers of people in your batch being one or the other that you're looking for. And so, the reason that this is important is because what whole genome sequencing has taught us is that each person is most impacted by somewhere around one to five super rare genes that they have, which means the older testing from 23andMe is not giving you anything accurate at that level.

So, the way we should think about our health is kind of like a double-layered cake — not that cake is the best thing for your health, but you've got one layer of the things that everyone should be doing. So, we should all be – You can mix some parameters around what is a healthy diet that anyone should be following. And we argue all the time about where those parameters are, but there are certain things that everyone would agree on, like eat mostly whole foods, make sure that you're meeting all the basic requirements for your nutrients, and so on. And then, we can argue about carbohydrate and fat, or whatever, but then there are other things that everyone should be doing, like stay active, get outside, get sunshine, et cetera, et cetera, et cetera. But then, there's this other layer, where it's things that are unique to me are going to be extremely unique to

me, because I've got a small handful of mutations that I could talk to 100 other people at a health conference and no one's going to have the same ones that I have.

And that, I think, is where you can unlock the big step after where all that commonality stuff gets you. In other words, none of it invalidates the things that we should all be doing, like getting the type of exercise we should be doing and eating a healthy diet, but it does make for us to be able to say, “All right, I've done everything that I can. I've achieved seven out of 10 for my health. How do I get to 10 out of 10?” And I think understanding those deep idiosyncrasies is how to unlock that last mile of the run.

Dr. Joseph Mercola:

Well, I'd like to challenge that supposition.

Chris Masterjohn, Ph.D.:

Yeah, go ahead.

Dr. Joseph Mercola:

So, you mentioned 14 million perturbations or anomalies, but there's only 23,000 genes. So, it makes it sound like there's more than there is. You can only have 23,000 genes that are in fact impacted, right?

Chris Masterjohn, Ph.D.:

Each gene – Yeah, that's fair. That's true.

Dr. Joseph Mercola:

Yeah. So, there's 23,000-

Chris Masterjohn, Ph.D.:

23,000 sites of variation in a – It depends how you look at it, right? So, there's one gene for numerous proteins, and so there's about 100,000 proteins, there's about 20,000 genes, there's about 14 million sites of variation.

Dr. Joseph Mercola:

Yeah. So, then-

Chris Masterjohn, Ph.D.:

Within 20,000 genes that make [inaudible 00:09:41]-

Dr. Joseph Mercola:

Obviously, there's enormous complexity that we won't even begin to learn in multiple generations after we're dead, because it's way too sophisticated and refined. But I think Bruce Lipton, Ph.D., had a really good take on this and its epigenetics, which is not so much that we're committed to some final complication because of our mutations, but it's the expression of those genes and the modulation of those genes. And we had talked on that [in] our last phone call, my recent fascination was carbon dioxide. How it modulates the function of proteins depending on the level of carbon dioxide in your body. It's a really important, pretty much unrecognized variable in optimization of health. And I understood that from Ray Peat, and he had an incomplete picture, because when I listened to a lecture from 2010 with Bud Weiss, he was saying how carbon dioxide modulates DNA, and carbon dioxide only attaches to proteins, specifically the lysine histidine residues.

So, I wonder how that could work, and then I realized it's the expression of the proteins on the genes, the histones – They are modulated. The histones modulate the expression of the DNA. So, if you can modulate in some way, we have no idea how or what they do, and how it's done. It's just an enigma. We just know that it does that. So, the supposition is that if you have this anomaly in the 14 million potential cases of the 23,000 genes, that's almost admitting that this is almost a fatal flaw. When it may not be, it may be there are other mechanisms that can bypass that, that we aren't aware of, because of the modulation of the histones. So, that's my retort.

Chris Masterjohn, Ph.D.:

Okay. Well, I think that definitely epigenetics is super important, but – So, genetics has a stronger impact on how each of us are different, and epigenetics has a stronger impact on, for example, if you have a unique problem, when in your life does it onset, and what is the power to resolve it? And it really doesn't have that much of an impact on how individual we are, because the types of epigenetic regulations are relatively narrow. So, you could say, for example, psychological stress is going to impact your epigenetics, but even though there might be – If you look at people's trauma, there are-

Dr. Joseph Mercola:

No, sure, that will.

Chris Masterjohn, Ph.D.:

Everyone's trauma can be very, very unique in terms of the experience of it, and what the content of it was. But there's not that many different types of stress response to trauma in the body. And so, the resulting epigenetics are largely narrow. So-

Dr. Joseph Mercola:

Well, I would challenge that.

Chris Masterjohn, Ph.D.:

Okay, go ahead.

Dr. Joseph Mercola:

I'm not accepting that as fact. Because the implied assertion is that we understand everything there is about this. And we don't.

Chris Masterjohn, Ph.D.:

That's true.

Dr. Joseph Mercola:

We don't know more than we know. And we both have been in this long enough to realize that there's innovations that are realized every year that completely turn our understanding of the situation upside down, and especially something as complex as the expression of our genes and behavior. And even with stress. Stress, I've seen many people. I even had a clinical practice, and I've seen literally stress destroy people. Absolutely destroy them. In ways that the most disciplined, motivated person is simply unable to recover from, until the neurological consequences of that stress, the circuits that got facilitated in their brain, are resolved. And there are energetic ways to do that, that are really astonishing and close to miraculous. But we don't know how it works, no one knows. So, I think it's almost a bit of hubris to imply that we do. We just don't know.

Chris Masterjohn, Ph.D.:

I'm not implying that we know everything there is to know. I'm implying that we've learned some things that are valuable.

Dr. Joseph Mercola:

Okay.

Chris Masterjohn, Ph.D.:

So, I think that when I say genetic, you are reading that as genetic determinism.

Dr. Joseph Mercola:

Yes. I think you're accurate. That was where perhaps I'm confused on your argument.

Chris Masterjohn, Ph.D.:

Yeah, I'm not saying that – If anything, I would argue against genetic determinism-

Dr. Joseph Mercola:

Oh good.

Chris Masterjohn, Ph.D.:

-because the point is to find the points of actionability.

Dr. Joseph Mercola:

Right.

Chris Masterjohn, Ph.D.:

If something's actionable, then by definition it's not deterministic, because your action is changing it. So, what I'm saying is, I'm not talking about determinism, I'm talking about uniqueness. And so, what I'm saying is – And granted, there are things we discover all the time. Like just a few days ago, it was discovered that mitochondria in axons of the brain do not produce ATP (adenosine triphosphate), but with a proton gradient, as described in the textbooks, bacteria do, and they consume ATP to generate a proton gradient, to generate [inaudible 00:15:22] protons. So, they work backwards according to what's in the textbook for humans, and they work – If you go to Wikipedia, it says ATP synthase-

Dr. Joseph Mercola:

That's a mistake.

Chris Masterjohn, Ph.D.:

Okay, fine. Don't go to Wikipedia. Go to molecular biology of the cell.

Dr. Joseph Mercola:

Yeah, that would be better.

Chris Masterjohn, Ph.D.:

It says that an ATP synthase is an FATP (fatty acid transfer proteins) running in reverse, because the original one consumed ATP to make a proton gradient in bacteria, and we've flipped it around. But they just discovered it last week, and the axons, they do it the original way. So, I'm not saying that we've reached the end of the road, and we now know everything.

Dr. Joseph Mercola:

I'm so glad. I thought you were smarter than that.

Chris Masterjohn, Ph.D.:

All I'm saying is that there are valuable things that we've learned very recently about the skew of genetic mutations in people that have actionable implications, which means that there's nuances you can add to how you do things to optimize and maximize your health. And my point about epigenetics is, obviously these things interact, but the epigenetics I really don't think adds as much about the uniqueness as the genetics do. Because we all can get stressed, but generally

stress is quite similar in what it's doing. There's a handful of stressors that we can experience — psychological and emotional, work, metabolic, not eating enough, exercising too much. There's a bunch of them, but they're relatively small.

Whereas, if you look at the skew of big bottlenecks in metabolic pathways, you're looking at 30-ish essential nutrients that could be altered, you're looking at three major macronutrients that could be altered, and you're looking at combinations that come from those, and that can give you really – You're really looking at thousands of possible individual bottlenecks that have maybe dozens to hundreds of implications of how you could uniquely tailor your diet. And it's not displacing all the other knowledge that we have, it's just adding something to it.

Dr. Joseph Mercola:

Okay. Well, let me ask you a clarification question.

Chris Masterjohn, Ph.D.:

Yeah.

Dr. Joseph Mercola:

Because the actionable items are going to be influenced by this, and that is the confidence you have in the reliability and reproducibility of this assay. I've read or heard some discussion that there's an issue there. That it's not as accurate as you may believe. So, what's your experience with that?

Chris Masterjohn, Ph.D.:

I think that you have to look at it in a couple of ways. So, what I do with my clients on [a] very small scale is, in depth looking at agreement between many, many, many different types of genetic and biochemical data, and the person's experience. What I think that people can do themselves in a more DIY approach is look at it as a hypothesis-forming experiment. So, to take an example, let's say that – I'll take an example from me. So, I found out that I have a riboflavin-responsive mutation, and I'm heterozygous for it. And in infants who are homozygous for it, there's an almost 100% infancy death rate, and they supplement them with riboflavin, and it abolishes 90% of that death.

So, I look at that, and I'm like, “Well, I obviously don't have that disease. I didn't die in infancy, but this might raise my riboflavin requirement.” And I just stumbled into the fact that supplementing about 75 milligrams of riboflavin immediately abolished my seasonal allergies, for example. I literally have not had any allergies since I did that. And there's many things that you should look at, but one of the things that you can look at is if you develop a hypothesis around it and you test it, what is the outcome?

Dr. Joseph Mercola:

Yeah. So, I'm just curious, in the riboflavin, what would you think the primary mechanism is? What's the bottleneck, or the function that gets disturbed? Complex II in the mitochondria, or is it something else?

Chris Masterjohn, Ph.D.:

It's actually Complex I. So, the gene is ACAD9, and ACAD9 is a moonlighting protein that fulfills two functions. One is in fatty acid oxidation, and one is as a chaperone to assemble mitochondrial respiratory chain complexes. And mechanistically, it's not fully mapped out exactly how it – Exactly what it does to assemble the respiratory chain complexes. And if you look at the case reports, it's usually Complex I that's deficient, but sometimes it's Complex II. So, to your earlier point, there's obviously a ton of work to do to still-

Dr. Joseph Mercola:

We don't know.

Chris Masterjohn, Ph.D.:

What the hell is going on, right? But I also had a respiratory chain assay from a cheek swab that, interestingly enough, did not show that I had a deficiency of anything, but it did show that my Complex II was way higher than my Complex I, which is not consistent with, "Oh, I have a disease." But it is consistent with the fact that I have a mutation that decreases Complex I. And I've actually found that super valuable, where, if I can just predict from a biochemical pathway, "Is this going to feed into Complex I more, or Complex II more?" I can consistently show that the things that feed into Complex II lower my resting lactate, and the things that feed into Complex I raise my resting lactate.

And also, that happens to be a very good leading indicator of a health effect. So, for example, I found that generally if something increases my lactate and I ignore it, it's going to wind up shortening my sleep. Whereas, if I remove the things that increase my resting lactate, and I take the things that decrease my resting lactate, generally, that improves other things I track such as my sleep.

Dr. Joseph Mercola:

I have a question on that, because I actually was planning on discussing this with you, because we both know that NAD (nicotinamide adenine dinucleotide), or specifically NAD+, is just a nightmare to measure. There's probably only a few labs in the world that can do it accurately, and it's only done within that lab. You cannot go to the blood draw station [and] think you're going to get an NAD measure. It's a fantasy, it doesn't work. So, we need surrogate measures of that. And NAD is probably one of the most important biomarkers around, no question. And your observation [is] that when you increase lactate, you are having problems with it. So, would it be fair to say that an increased lactate would be – I believe lactate is reduced and pyruvate is oxidized? Is that correct? From the redox perspective?

Chris Masterjohn, Ph.D.:

That's correct. Yeah.

Dr. Joseph Mercola:

Yeah. So, when you have increased lactate, that would suggest that you have an increase in the reductive stress of sorts, which it sounds like you're experiencing. And you would have an increase in NADH (nicotinamide adenine dinucleotide hydrogen), and your NAD+ ratio would go down. So, all of that is the framework to asking the question, do you think that lactate-to-pyruvate ratio is a good correlated surrogate marker for NAD+ levels? Which is impossible to measure almost.

Chris Masterjohn, Ph.D.:

So, I actually don't even think it's necessarily desirable to try to measure NAD+, and-

Dr. Joseph Mercola:

A lot of people do it, there are supplements for it. And the justification for the use of these supplements [is] they have measures that it increases NAD levels.

Chris Masterjohn, Ph.D.:

Yeah, I've written a review of why I would not use that test, so-

Dr. Joseph Mercola:

I'm sorry I didn't see it, I wish I would've [inaudible 00:23:53].

Chris Masterjohn, Ph.D.:

No, I can send it to you. So, my website is chrismasterjohnphd.substack.com, and in the menu there's a button that says lab tests. If you click on lab tests, then there's a section that says reviews of lab tests, and that's where you'll find my review of that lab test. So, the problem with that lab test is that it is misunderstanding that the real point is what you were just talking about, which is about the redox status of NADH, more than it is about the amount of NAD+. And there's another aspect of it, where it is true that with aging and disease status, you accumulate DNA damage, and during the DNA repair process, you hydrolyze NAD+, and completely break it down in order to tag that DNA for repair.

It's not even involved in the repair process. It's like a labeling process for the DNA repair. And there are other enzymes that hydrolyze NAD. For example, there are derivatives of NAD that are used as neurotransmitters, which involves the irreversible hydrolysis of NAD, and the sirtuins and other enzymes involved in telomere metabolism and so on. But the correlate[ion] of aging and disease status is really the use of PARPs (Poly (ADP-ribose) polymerase), which are the enzymes that irreversibly hydrolyze NAD to repair DNA. And so, the more DNA damage that you have, the more NAD you hydrolyze. And so, the people that are saying, “Well, young people have X amount of NAD, and so you can calculate your biological age by how much NAD you

have, and that can tell you whether you need to supplement with NAD precursors," that's getting only the aspect of the DNA damage, and it's totally missing the point that the DNA damage is not caused by NAD+ deficiency. It's causing the NAD deficiency, and it's caused by oxidative damage. Right, so you're using-

Dr. Joseph Mercola:

Or reductive stress. An excess of electrodes.

Chris Masterjohn, Ph.D.:

Okay, so first of all, I don't – I'm an anomaly here, but I really hate the distinction between reductive and oxidative stress, for a couple of reasons. So, first of all, by definition – and this is chem 101. By definition, all these reactions are called redox reactions because every reduction involves an oxidation and vice versa, so you can't have a reaction that's a reduction without an oxidation. And then, further, health is defined by having really strong polarization of different compartments' redox status. So, in general, you want a very reduced glutathione pool, and you want a very reduced NADPH (nicotinamide adenine dinucleotide phosphate) pool, and you want a very oxidized NAD+ pool. And when you get unhealthy, you don't get more reduction, you get closer to chemical – Chemical equilibrium is death.

And chemical equilibrium means that everything is randomly mixed together. So, rather than having the polarization of very reduced NADPH and very oxidized NAD+, you wind up getting mediocre middle ground on all of them. So, if you look at a diabetic, they're not all across the board reduced. Their glutathione pool is too oxidized, their NADH is too reduced. So, I know where you're going, and I think you're right, I just don't like the term – I don't like to distinguish.

Dr. Joseph Mercola:

[inaudible 00:27:42]-

Chris Masterjohn, Ph.D.:

It's all the same thing, right?

Dr. Joseph Mercola:

It's really semantics for the most part. So-

Chris Masterjohn, Ph.D.:

Well, yes, but semantics comes from the Greek, "semantikos," which means important.

Dr. Joseph Mercola:

Okay. This is all a rabbit hole from what my original question was, what do you think of using the lactate-to-pyruvate ratio as a marker, a surrogate, that you could use to get some good information about the redox status?

Chris Masterjohn, Ph.D.:

Right. Real quick to finish that point up, you and I are in agreement. I'm just saying that oxidative stress and reductive stress are two sides of the same process.

Dr. Joseph Mercola:

Okay.

Chris Masterjohn, Ph.D.:

So, generally speaking, lactate-to-pyruvate ratio is going to reflect the cytosolic redox ratio of NADH, NAD+, and the beta-hydroxybutyrate-to-acetoacetate ratio is going to reflect the same thing in the mitochondria. And so, if you measure both, you can get more insight into how those are compartmentalized. There are a lot of drawbacks to the different ways that you can test this. For example, if you were in a clinical setting, and you were really trying to infer something very specific and important about those things, you would probably be drawing arterial blood to be able to see what's happening in the arteries instead of the veins. Whereas, there's going to be arterial venous differences, meaning if you get a venous blood draw, and then if you get a finger prick, you've got capillary blood, venous, arterial and cells mishmashed into it.

So, you're not going to see all these things reflect exactly the same thing, but this is generally true, and you can also measure them in urine, it's just much less precise. The problem with the home measurement is no one has a measurement for pyruvate or for acetoacetate at home, and I really do think it could be developed quite easily, because it's actually way easier to measure it right away than it is to measure it – When they do a venous draw, there's all sorts of stuff they have to do to stabilize it, because they're not doing the assay right away. So, I hope someone develops a home monitor-

Dr. Joseph Mercola:

Yeah, because they have home monitors for glucose, and pyruvate is half of glucose, so it shouldn't be that hard.

Chris Masterjohn, Ph.D.:

Right. I heard that Abbott is making a continuous glucose, ketone, [and] lactate monitor, which would be amazing, because right now I do glucose, ketone, [and] lactates with two different fingerprint meters. But I really wish they could have pyruvate and acetoacetate in it because those give you the ratios. And so, the problem with just using lactate as a stand-in for the lactate-to-pyruvate ratio is that it doesn't control for the rate of glycolysis. So, if you have an adrenal stress response, your lactate is going to go up, but your lactate-to-pyruvate ratio is going to stay

the same. And so, it's like at home, it is hard to tell the difference between an increase in glycolysis versus a slowdown in NADH oxidation.

But if you collect enough data you can start to make sense of it. For example, if I supplement with high-dose thiamine, and my resting lactate goes up and I feel calm, it's not an adrenal response. That thiamine is just clearly increasing the NADH beyond what my respiratory chain can oxidize. And so, I can use that resting lactate and basic biochemical sense to say, "This is too much thiamine for me at this time."

Dr. Joseph Mercola:

Okay, good. Thank you.

Chris Masterjohn, Ph.D.:

Yeah.

Dr. Joseph Mercola:

So, I guess-

Chris Masterjohn, Ph.D.:

So, in a more general sense, I think one of the things that people can do to – This is what I'm saying. I'm not saying whole genome sequencing is perfect and the end of the story, therefore everyone should get it, read the report, and do what it says. But what I'm saying is that, now that we know that it's as common to have something that might require high-dose thiamine, as it might be to require high-dose riboflavin, as it might be to have an impairment in Complex I, or a need for riboflavin to fix Complex I, if we understand that the skew is such that all these problems with this level of resolution is actually very common and different between people, then all of a sudden the rationale for testing your home lactate along with your home glucose becomes very strong.

Because you can say, "You know what? My primary limitation might be in the respiratory chain. If I'm supplementing with something like thiamine or biotin, that plays no role there, but does put more stress on the respiratory chain by helping me break down branch-chain amino acids, or carbohydrate, or whatever" then all of a sudden it becomes real sensible to say fasting lactate is a great way to see that imbalance. It's not perfect, but it's the best thing you can do at home, and you can start to get much more resolution and also leading indicators. So, it might take two months to realize that something's been chopping away at your sleep five minutes every night, whereas if you saw your lactate spiking the first day that you used it, you could have gotten a leading indicator on that and avoided that problem.

Dr. Joseph Mercola:

So, do you think that the home blood lactate levels, which are kind of pricey, $4 or $5 a test, compared to-

Chris Masterjohn, Ph.D.:

They're like a $1.15 a test.

Dr. Joseph Mercola:

Oh, okay. I thought they were higher. Sorry.

Chris Masterjohn, Ph.D.:

Well, it might depend on the company. I use Nova Biomedical Lactate Plus.

Dr. Joseph Mercola:

Okay. So, that's reasonable. Do you think they're more accurate than the commercial lab, because there's a lot of details? I was actually going to probably do it tomorrow. Where you have to freeze the tube, you refrigerate it right after you draw it, and then spin it down instantly, and separate the plasma.

Chris Masterjohn, Ph.D.:

[inaudible 00:33:45]-

Dr. Joseph Mercola:

What do you think is more accurate?

Chris Masterjohn, Ph.D.:

The only issue with a lactate-to-pyruvate ratio at a commercial lab, the only issue that really matters, is that they mix 4 ml of the plasma – of the whole blood, not plasma – 4 ml of whole blood with 4 ml of ice-cold perchloric acid, and let it stand for 10 minutes before they centrifuge it. And they have to mix it with the perchloric acid right away, and that prevents pyruvate from being converted to lactate. It's-

Dr. Joseph Mercola:

So, you can measure pyruvate at a lab, I didn't think they had it. I couldn't find it.

Chris Masterjohn, Ph.D.:

Boston LabCorp has it.

Dr. Joseph Mercola:

They do? I couldn't find it on LabCorp at all.

Chris Masterjohn, Ph.D.:

Well, if you go to my website, and you get a lab tests, and you click on comprehensive screening for energy metabolism, I think there's either a clickable link or a code [inaudible 00:34:40]-

Dr. Joseph Mercola:

They have it, okay.

Chris Masterjohn, Ph.D.:

Yeah.

Dr. Joseph Mercola:

Okay.

Chris Masterjohn, Ph.D.:

But it's not an either or, right? So, first of all, you got to know what the phlebotomist has to do and tell them. What I did is I printed out the Quest instructions, and then I walk in and tell a phlebotomist, "My doctor said it was super important that you follow these instructions, do you have this here? Are you going to do it this way?" And that led to 20 minutes of the phlebotomists talking to each other, and looking up stuff on the computer, and then telling me they were going to do it wrong. And then me saying, "Are you sure? Read this thing". And them saying, "Oh yeah, you're right." And they did it right, but it was a hassle.

Dr. Joseph Mercola:

Wow.

Chris Masterjohn, Ph.D.:

And then, you wind up with the problem that there's always questions about did they mess it up.

Dr. Joseph Mercola:

Because human error.

Chris Masterjohn, Ph.D.:

But you can't measure pyruvate at home, you just can't do it. So, I don't like to put all my faith in any one test, but what I do like to do is measure the lactate from the meter, and – Obviously you can't run Quest lactate-to-pyruvate ratio every day, whereas $1.15 versus that hassle, it's like – Right?

Dr. Joseph Mercola:

Yeah, that's two hours out of your life.

Chris Masterjohn, Ph.D.:

Right. Let's say a practical thing is you're trying to optimize something, you have a hypothesis about how it's supposed to go, you expect that your lactate-to-pyruvate ratio will improve over the course of three months if you do it right, then what you want to do is basically calibrate your home lactate to the Quest or LabCorp lactate-to-pyruvate ratio, and ideally, you probably want to do the finger prick at the same time. And you're not trying to correct them, or use them to correct you, you're trying to look for the agreement. Because you are not measuring your vein, you're measuring your finger prick, which is different, and they have the process that is standing before it's analyzed and stuff.

So, what you're trying to do is say, "Okay, when my home lactate was an average of 1.2, my lactate-to-pyruvate ratio measured by the lab was high at 25. And then, when I did X, Y and Z that I expected to improve my respiratory chain function, dropped my average home lactate down to 0.7. My lactate-to-pyruvate ratio at LabCorp or Quest went down to 7, which is in the ideal range." And then, you can look at the agreement of those things, and you're calibrating them to each other knowing that neither is perfect, but the more corroboration you have the more confident you are.

Dr. Joseph Mercola:

So, how confident are you that the lactate-to-pyruvate ratio, which I think was really the original question, going back to it, how confident are you that's a useful assay to imply a functional status if it's in an optimal range, like 7? Is that a good marker that you think that people should strive towards or be concerned if it's not there?

Chris Masterjohn, Ph.D.:

I would say that – Well, I'll give you an interesting case from my experience. So, before I really had my system developed for how I would approach genetics now, I was looking at stuff and trying things, and I thought I would be a good candidate for high-dose biotin. And-

Dr. Joseph Mercola:

Was that for oxalates that you were doing that?

Chris Masterjohn, Ph.D.:

No.

Dr. Joseph Mercola:

[inaudible 00:38:25].

Chris Masterjohn, Ph.D.:

No. Interestingly, I have a hypothesis that biotin helps convert oxalate to carbon dioxide.

Dr. Joseph Mercola:

Yeah, yeah.

Chris Masterjohn, Ph.D.:

Yeah.

Dr. Joseph Mercola:

Maybe we should talk about that, if we have time.

Chris Masterjohn, Ph.D.:

Yeah. Okay. But I was reasoning based on symptoms, based on past supplements that had harmed me, and based on genetics suggesting my biotin recycling was poor, and also based on just – I tested a bunch of stuff, and my biotin intake was really high, and my blood level was pretty low, and I didn't think it made sense with what I was eating. So, I thought the recycling gene makes a lot of sense, I probably need to do a biotin-loading phase. And interestingly, I knew about the ACAD9 mutation, which is the riboflavin-responsive respiratory chain problem, but I dismissed it because all of my ratios of everything looked oxidized and I thought I don't have a respiratory chain issue. My lactate looks good, my beta-hydroxybutyrates, all those ratios looked oxidized, they didn't look like I had a respiratory chain problem.

Okay. So, I do 10 milligrams of biotin a day for about a month, and by the end of the month, I'm walking into a room two or three times a day and forgetting why I walked in. I am a naturally clumsy person, but at the end of that month, I was like – I'd be holding my phone, and it would fly out of my hand, and I'm like, "How did that happen?" And I was getting very easily angered. So, I was in a conversation where the stress of the conversation would otherwise have been very trivial, but I got so angry that I screamed so hard that I saw stars. And the only time I've ever seen – not stars, but flashing lights – the only time I've ever experienced that in the past has been through physical stress.

The first time was when I was deadlifting heavyweight, and then there have been times where I've been weak and I lift something that I didn't think would cause that, and it did. I've never gotten angry and had that happen. So, I'm assuming I had an insane blood pressure spike at that point. And then, I had a glass of wine with my mom around the holidays, and one sip of wine was making my hands tingle. And I was like, "Okay, I'm going to stop drinking it, I'm going to wait a little while, it would go away." I'd take another sip, the tingling comes back. And in the morning, after I drank a half a glass of wine, my lactate was 4 [millimole per liter]. 4 millimole per liter lactate is insanely high; it should be under 1[millimole per liter].

And so, then I got off the biotin and everything withdrew. I was noticing that my lactate was going up the whole time, and I was just saying, "You know what? I don't think it's going up that much, it's not a big deal, I think I need this." I rationalized it. But at the very end, before I stopped, I redid all the lab tests that I had done originally, and all of a sudden it looked like I had a respiratory chain disorder. And so, to me, that's remarkable agreement. And I was looking at

the venous blood ratio as well as the ketone body ratios and lactate-pyruvate ratios and two organic acid tests.

And basically, I was like, “Oh, the respiratory chain issue was there all along. I just needed to put some stress on it to discover its relevance.” And looking back on that, I could have not trivialized the rise in my resting lactate that I was observing happening in real time, and I could have said, “This is probably a bad sign. Let me back off to a lower dose.” And then I would've avoided all of those problems. And I noticed the problems developing too, but I was very committed to getting the post-biotin lab data, for the sake of science. If I wasn't committed to the scientific experiment, I probably would've stopped it a week earlier or something. But the point is, I could have used the home lactate as a leading indicator before I noticed any of the neurological problems, and gotten rid of it earlier.

And so, I think, if you are content with just eating well and exercising well, and everything's going well, and you're not trying to optimize, and you're not trying to fix a problem, then fine, whatever. But no one needs to be on 10 milligrams of something that the requirement is 30 micrograms of, unless they have a very unique need for that. Speaking of determinism, there's a gene mutation, a very severe homozygous biotin-related disease, where this one mutation was considered an absolute death sentence in infancy, and no one had ever said maybe more than the traditional 10 milligrams of biotin for a genetic disorder in biotin metabolism is needed. And then, someone decided to say, “I've got one of these girls who has this mutation, she's supposed to die any minute now. I'm going to keep titrating the biotin up until her skin rash goes away.” So, they did that, and then she wound up on 1.3 grams of biotin a day.

Dr. Joseph Mercola:

Which is 1,300 milligrams.

Chris Masterjohn, Ph.D.:

Right. So, 10 milligrams gave me a neurological disorder, and 10 milligrams is insanely high compared to the 30 to 300 micrograms. You can debate it, what the basal requirement is. She's on 1.3 grams instead of 10 milligrams, 130 times what I was on. But last time anyone published on her, she was alive at 13 years old, which is considered impossible, according to the textbooks on this disorder. And so, it's very clear that you can need – Now, my perspective is, if you were heterozygous for that mutation, you would not die in infancy, but you would probably have-

Dr. Joseph Mercola:

Increased requirements, for sure.

Chris Masterjohn, Ph.D.:

Increased requirements. And so, you are operating outside the realm of medical diagnostics when you are looking at that, because you can go to an inborn error of metabolism specialist and they're going to turn you away. They're going to say there's nothing wrong with you. There's a really interesting case report of a woman who was – She'd been pregnant twice, if I remember

correctly. She was about 38 years old, and she started developing chronic vaginal yeast infections that were not responding to treatment. And she, luckily enough, knew that she was heterozygous for a biotinidase mutation, which is the enzyme that recycles biotin. The reason she knew this is because her husband also had it, and her child was diagnosed with the disorder, and was on 10 milligrams of biotin for life. So, she called up the genetic counselor, and she said, "If my son needs 10 milligrams of biotin, is it possible that I need 10 milligrams of biotin too, and this is why I'm getting all these yeast infections?" And the genetic counselor said, "I don't know, try it." So, she takes 10 milligrams of biotin, the yeast infections go away.

Dr. Joseph Mercola:

[inaudible 00:45:56].

Chris Masterjohn, Ph.D.:

So, there is a need to experiment outside the boundaries of diagnosable diseases, and in the realm of optimization. But my point is, once you get into optimizing with things that are outside the realm of "everyone should do this," that's the point where you really want to take additional measures to test whether you are actually optimizing what you think you are. And some of these things, like testing your resting, fasting glucose, ketones and lactate, can give you a lot of color on – They're not going to pinpoint an exact issue, but just knowing whether you are overstressing your respiratory chain for one of 300 reasons is a huge thing to know, because it allows you to say, "I know that." Because you're not just looking at whether it's high, you're looking at what to it.

So, if you put in biotin at 5 milligrams a day, and your lactate goes from 0.7 to 2 millimoles per liter, you know that biotin overstresses your respiratory chain. You don't know with exact precision about why, but you don't need to to say, "That's too much biotin for me. That was an error in my optimization, and I'm going to pull back, and then I'm going to figure out my next plan of action."

Dr. Joseph Mercola:

Yes. So, I guess generally we've gone deep in the weeds without really giving some broader recommendations. Because you treat patients – Well, patients, clients, I guess, because you're not-

Chris Masterjohn, Ph.D.:

I don't treat any patients. I'm not a doctor.

Dr. Joseph Mercola:

Right. Yeah, that's right. But you coach people, I guess, might be more accurate, with respect to implementing these recommendations. So, I'm wondering the strategy that you've adopted and chose to use, with respect to optimizing what the well-recognized requirements are for health, the Weston Price principles and Ray Peat and all those, and getting them on board first, see where

they equilibrate, and then see what's left over before you start looking at these. It seems to me that would be a wise strategy initially.

Chris Masterjohn, Ph.D.:

Oh, yeah.

Dr. Joseph Mercola:

Because even if it didn't do it, you'd have to do the basics. What you're talking about is a refinement, and if you ignore the basics, they aren't going to work. You've got to hit the foundations.

Chris Masterjohn, Ph.D.:

Well, even worse than that, if you get into the mindset that you don't need to do the basics because you found some holy grail for your personal individualization, it can really trap you into disregarding the basics until it hurts you.

Dr. Joseph Mercola:

[inaudible 00:48:45] over the head.

Chris Masterjohn, Ph.D.:

I've seen it happen like, “Oh, I have a very high need for carnitine? Cool, I'll have pizza and carnitine tonight. Ah, that worked fine, I'm going to do it the next day.” And so, you definitely – Yeah. Like I was saying before, it's a two-layer thing – Think of it as a house instead, that's better than a cake. If you didn't build a foundation, your house is going to fall down. I don't care how sophisticated your architecture was when you made the top of the house. The roof looks amazing, but if there's no foundation, it's not going to look amazing when the storm comes.

Dr. Joseph Mercola:

Yeah, that's right.

Chris Masterjohn, Ph.D.:

So, no, I very much agree with that, and if you want we could talk about that, although I imagine you talk about that a lot, right?

Dr. Joseph Mercola:

I do, but I've never interviewed you before, at least I don't think I have. I don't recall. So, I'm not really quite familiar with your strategy, other than you initially embraced Weston Price's work, and I suspect you – Or Weston Price Foundation. Maybe Weston Price, I don't know what's more accurate. And there's some broad general principles there I think would be really hard to refute

by anyone. But I just wondered what you consider the basics, and what you would like to see people doing before you start investigating these advanced strategies. We can maybe dialogue [about] that.

Chris Masterjohn, Ph.D.:

Yeah. Well, I would say, I believe in a lot of basics, or low-hanging fruit, 80/20 rule, or whatever you want to call it.

Dr. Joseph Mercola:

[inaudible 00:50:21].

Chris Masterjohn, Ph.D.:

Some of them are very high evidence, and some of them are speculative, but I believe them anyway. And some of them have limited evidence. So, I would say, some of the very high evidence things are, you want to eat a diet that gets all of your basic nutrients, your basic micronutrient targets from food. And that one rule will make you eat mostly high nutrient density whole foods because you are not going to hit the RDAs (recommended dietary allowances) for the basic nutrients if you are eating junk food. And I guess, a conventional nutritionist would disregard whether they're actually coming from food or not, but I would say exclude fortified foods and multivitamins, and ensure that you're getting from the naturally occurring micronutrients in all the foods, that you're hitting on those targets.

And I think that it imposes on you a dietary framework that is automatically pretty decent in terms of the breadth of whole foods that you're eating. I think a lot of people would benefit from tracking their micronutrients in an app, such as Cronometer, for at least a representative period of time, just to get a-

Dr. Joseph Mercola:

Maybe more.

Chris Masterjohn, Ph.D.:

Just to see what you're eating, and whether you are hitting those targets.

Dr. Joseph Mercola:

I like Cronometer for finding the metabolic poisons in your diet, with the primary one being linoleic acid. Because I talked to Aaron Davidson, who is the founder of that app, and convinced him to include an omega-6 meter.

Chris Masterjohn, Ph.D.:

Oh, cool.

Dr. Joseph Mercola:

Yeah. Because the lower you get that, the better. I think that's one of the most important ones. And I suspect, and I'm quite certain that you've reviewed that before, but I haven't done a deep dive on your work, so I don't know where your position on that is.

Chris Masterjohn, Ph.D.:

Yeah. So, I think it becomes super – It's relatively easy to say avoid seed oils and consume traditional fats, kind of the way Weston Price does. Like, to the extent you use added fat, used butter, olive oil, tropical oils, animal fats and so on. It gets a little bit more difficult if you're dealing with something like chicken or pork, where the way that the animal is raised and what it's eating has a huge impact on composition.

Dr. Joseph Mercola:

99.9% of them are raised that way.

Chris Masterjohn, Ph.D.:

Right. Well, so the thing is, it's very easy to say, "Use these oils, not those oils." It's hard if you're eating a pastured chicken to know whether to trust the USDA database in Cronometer, for the linoleic acid content, which is probably going to be too high for your and my taste.

Dr. Joseph Mercola:

Well, the problem with pastured chickens – and I'm a good friend and supporter of Ashley Armstrong, who's probably the premier expert in raising chickens in this country, and has actually identified the ideal chicken diet, believe it or not. It's really not what almost all pastured chicken consumes, that they are getting foods that are relatively high in linoleic acid, and they have pretty – Levels up to 20-

Chris Masterjohn, Ph.D.:

[inaudible 00:53:49] diet, acorns and coconuts?

Dr. Joseph Mercola:

Yeah, yeah. Well, no, ideally they're supposed to eat bugs as their primary protein source, and then supplement with carbohydrates and maybe some other thing, really low-LA grains, like white barley. But there's very few that do this. You have to be really-

Chris Masterjohn, Ph.D.:

There are people that are specializing on marketing low-PUFA (polyunsaturated fatty acids) pork and chicken.

Dr. Joseph Mercola:

Yeah, yeah. You know one of the best ways to get really low-PUFA pork, really close to under 1%?

Chris Masterjohn, Ph.D.:

What?

Dr. Joseph Mercola:

It's a byproduct of making butter. What do you have leftover when you make butter from milk? Well, skim milk.

Chris Masterjohn, Ph.D.:

Right.

Dr. Joseph Mercola:

With virtually no fat.

Chris Masterjohn, Ph.D.:

Yeah.

Dr. Joseph Mercola:

It's half a percent, right?

Chris Masterjohn, Ph.D.:

[inaudible 00:54:36] butter with cheese, but anyway.

Dr. Joseph Mercola:

So, that's what you feed the hogs, and you get really high saturated fats, virtually no PUFA.

Chris Masterjohn, Ph.D.:

Yeah, that makes sense. Isn't that kind of common even on-

Dr. Joseph Mercola:

Well, it used to be common 100 years ago, but it's not done now at all, hardly.

Chris Masterjohn, Ph.D.:

Well, but this really is – it's very hard to optimize the PUFA content in your meat compared to ditching the crappy oils and-

Dr. Joseph Mercola:

Well, it's not that hard, you just restrict-

Chris Masterjohn, Ph.D.:

[inaudible 00:55:11], it's hard.

Dr. Joseph Mercola:

Just restrict it to ruminant animals. But now, I don't know if you've heard of this. This is a complete perversion and bastardization of the food system. There's this belief that PUFAs are healthy, so the food scientists have created ruminant-resistant fats. Essentially, it's time-released fats that bypass the rumen to go into the small intestine, and – I think that, yeah, small intestine. And they absorb it there. So, they have high PUFA levels. Even the ruminants. They destroyed the ruminants' capacity to saturate those fats.

Chris Masterjohn, Ph.D.:

Do you know why vitamin E is called tocopherol?

Dr. Joseph Mercola:

It's a fertility factor.

Chris Masterjohn, Ph.D.:

Yeah. And the only known role whatsoever of vitamin E is to protect PUFAs from lipid peroxidation.

Dr. Joseph Mercola:

Yeah.

Chris Masterjohn, Ph.D.:

So, [inaudible 00:56:05]-

Dr. Joseph Mercola:

In my view, virtually everyone watching this is high in PUFAs, and I think they're out of their mind if they're not taking a decent dose of vitamin A. Not excessive, you don't need a lot, 100 or 150-

Chris Masterjohn, Ph.D.:

No, but your vitamin – So, people who choose supplemental vitamin E are generally getting too much. And the data indicate that 0.6 milligrams of vitamin E per-

Dr. Joseph Mercola:

[inaudible 00:56:31].

Chris Masterjohn, Ph.D.:

-gram of PUFA in the diet is what you need to be protected. But if you consume PUFAs for four years or more, your vitamin E requirements stays at the level that the PUFAs drove it to then for four years after going low PUFA. And if you go low PUFA, your vitamin E intake actually drops, depending on what you're eating. It can drop, like coconut oil-

Dr. Joseph Mercola:

Yeah, because most of the vitamin E in foods is from high-PUFA foods.

Chris Masterjohn, Ph.D.:

Right. But if you take the vitamin E to PUFA ratio of the food, then you can organize them differently. And that's definitely worth looking at in Cronometer, whether you're getting 0.6 milligrams of vitamin E per gram of PUFA. But also, if you just take the ratio in a nutritional database, you can see that, for example, palm oil is rich in vitamin E and it's way higher than vitamin E-to-PUFA ratio. And even grass fed butter is fairly high for vitamin E-to-A ratio. And you look at something like wheat germ oil, it's really high in vitamin E, but the ratio to PUFA is not that high. But people who don't understand these things, who are just eating regular trash food, it's very easy for those people to go from seed oil heavy diet to coconut oil and not realize that their vitamin E requirement is-

Dr. Joseph Mercola:

Still high.

Chris Masterjohn, Ph.D.:

-still high for four years after that because of what they used to eat.

Dr. Joseph Mercola:

Yeah. It probably isn't even a little bit longer. It depends on a lot of variables, how low it goes, and some other components, but-

Chris Masterjohn, Ph.D.:

I'm just basing that-

Dr. Joseph Mercola:

The half-life is 650 days.

Chris Masterjohn, Ph.D.:

There were some experiments back in the day where they did adipose tissue biopsies over the course of years, and it's tough to say exactly, because we don't have a lot of data from different levels of restriction and how that influences the rate, but I would say the rule of thumb is about four years, and yeah, it could be longer, shorter, depending on your metabolism, and how much you restrict versus moderate the fats and stuff.

Dr. Joseph Mercola:

Yeah. So, you have seed oil restriction as one of your basics, I would assume?

Chris Masterjohn, Ph.D.:

Yeah. At some point it comes in to have to make decisions of trade-offs. Because I do think it makes sense, for example, if out of the foods that you are willing to eat, if you find that nuts are a major source of magnesium, it might be worth it to eat the nuts. If you're willing to eat whatever works – if I eat nuts, I eat macadamia nuts because they're very low in PUFA, and they're also very rich in minerals.

Dr. Joseph Mercola:

That would be the way to do it.

Chris Masterjohn, Ph.D.:

Although, too many nuts of any type is going to give you too many anti-

Dr. Joseph Mercola:

Two walnuts are 5 grams of linoleic acid. Two walnuts.

Chris Masterjohn, Ph.D.:

Yeah, I really-

Dr. Joseph Mercola:

It's more than any human should have. Probably one is the limit. And of course, if they're eating food, they're going to get linoleic acid. It's even in watermelon. I eat 4 pounds of watermelon sometimes, and I get a gram of linoleic acid.

Chris Masterjohn, Ph.D.:

Yeah, but that's probably in the seeds that come out in your poop.

Dr. Joseph Mercola:

Well, I don't typically don't eat the seeds, but I'm not-

Chris Masterjohn, Ph.D.:

No, but I'm saying if you measure the watermelon in a nutritional database, it's probably going to tell you what is in the seeds that don't come up.

Dr. Joseph Mercola:

Ah, I didn't consider that, that probably is accurate. Yeah. Because they probably digest the whole food.

Chris Masterjohn, Ph.D.:

Right. Yeah.

Dr. Joseph Mercola:

Yeah.

Chris Masterjohn, Ph.D.:

For sure. Yeah. The nutritional databases, they'll try to collect the edible portion, but that doesn't mean that they adjusted for what didn't get absorbed, or even broken down at all.

Dr. Joseph Mercola:

Yeah, yeah, yeah. People are not going to-

Chris Masterjohn, Ph.D.:

The corn on the cob value in the USDA database is not counting how many corn kernels came out in the poo the next time.

Dr. Joseph Mercola:

No, they're not. So, a few other things. Two things I like to talk about is protein, you said as long as you get the macronutrient value. Well, protein is an interesting component, and the Weston Price, I think is totally accurate, with [the] suggestion of eating nose to tail, which would include the connective tissue in the organs. And hardly anyone is eating connective tissue. It used to be common, and people used to eat it indirectly in Jell-O, and that's not really a common treat anymore. But it seems to me, I'm coming more to realize the importance of the microbiome and the support of that. And I'm sure you're familiar with the GAPS (Gut and Psychology Syndrome) diet, which was popular a decade and a half ago, maybe two decades ago.

But the crux of that was bone broth, which is probably the most magnificent form of collagen, which is far better than extracting it from hides and hooves. So, what role do you place bone broth in, properly made bone broth? Which is easy to do. The problem when I did [Dr.] McBride's work, almost everyone says, "I'm not going to cook bones for two days in a cook pot, on the stove, it's just not going to happen. It's too dangerous, and too much attention, too much energy production." But you can make it in an Instant Pot, seamlessly, with pressure and heat for four hours, and you just press a few buttons and it's done in four hours. You don't even have to look at it.

Chris Masterjohn, Ph.D.:

Yeah, I have made bone broth that way before. I do generally find that I get more done if I don't do any cooking at all.

Dr. Joseph Mercola:

Wait, wait, wait. Expand on that. That is an interesting anomaly. So, you don't cook at all, you just eat raw?

Chris Masterjohn, Ph.D.:

No. Okay, so I have an assistant who comes in five days a week and prepares my food, and I guess I could have her make bone broth. But I actually get – I have an Amish farm that makes bone broth, and just ships it with other foods on dry ice to me, once a week, so I just outsource it to-

Dr. Joseph Mercola:

Where are they? In Pennsylvania?

Chris Masterjohn, Ph.D.:

They're in Pennsylvania, yeah.

Dr. Joseph Mercola:

It's a long trip to Miami.

Chris Masterjohn, Ph.D.:

They just UPS it on dry ice. And it's higher-quality food than I would get if I was doing a Whole Foods delivery, or-

Dr. Joseph Mercola:

Oh, sure. That's about it, they really have established the bar for high-quality food, for sure.

Chris Masterjohn, Ph.D.:

Yeah. Anyway, your question was what do I think about bone broth? I think, generally speaking, I would say that one of the important metrics is the methionine-to-glycine ratio in the diet, and if you optimize around that, the rule of thumb is, really, you want to eat all the bones and collagenous tissue that would be associated with the meat that you're eating.

Dr. Joseph Mercola:

Yeah, and hardly anyone does, that's why I mentioned it. It's very rare to find someone that's doing that. It's very rare.

Chris Masterjohn, Ph.D.:

Yeah. My problem with doing it at home is, as I try to optimize an efficient system for my food generation, I find it super easy to do that if I cook a chicken in the Instant Pot, and then I take the whole chicken, take the meat off, and throw the bones back in. But like we were talking about before, there are drawbacks to focusing on chicken, and-

Dr. Joseph Mercola:

Well, I would-

Chris Masterjohn, Ph.D.:

If you're dealing with a ruminant, it's a lot of work to think – You really are not going to think like, "Oh, this much equals a cow, and there is this much bone-"

Dr. Joseph Mercola:

No, no, no, I agree. So, you get a dose of collagen. And you wouldn't be cooking all the cow bones, there's some that are particularly useful, which are typically knee joints. And they're called knuckle bones, go figure why they call them that, but that's what they call them, as the butcher would call them. But the source of collagen of those are just through the roof. It's the most magnificent collagen you can get.

Chris Masterjohn, Ph.D.:

Yeah. As a general rule of thumb, I would say you generally want 10 to 15 grams of collagen for at least every 100 grams of non-collagen animal protein. If you eat a more plant-based or shellfish-based diet, your methionine-to-glycine ratio starts to look a lot like what it would look like if you ate [an] animal diet, nose to tail. So, I do think it's very much the degree to which you need to think about drinking bone broth as a minimum target is very dependent on-

Dr. Joseph Mercola:

The food you're eating.

Chris Masterjohn, Ph.D.:

-how much meat you're eating. You want to think about it a lot more when you're eating a lot more meat.

Dr. Joseph Mercola:

Yeah. But there's still value for glycine. Glycine has gotten a lot of [inaudible 01:05:52], I'm sure you're aware, it's a really potent longevity correlation.

Chris Masterjohn, Ph.D.:

It does a lot of things. It helps sleep, it helps blood sugar, it's super important for the startle reflex. One thing that I think people will tend to dismiss and not think "what does this mean" is if someone is easily startled more than they should be, they're probably low in glycine.

Dr. Joseph Mercola:

Yeah. That's a good point. And it's a really inexpensive and easy one to take. I think what Ray Peat was recommending – he recommended mostly people get it from – well, from not collagen, [but] gelatin. Which is not as healthy typically as collagen, but even far less healthier than bone broth, which I think is the ideal. Because he had some concern about the supplements being made back then. But I think there's been improvement in the manufacturing quality of the supplements produced. So, glycine nowadays is actually acceptable. I think when Peat was advocated it wasn't. They had some problems making it.

Chris Masterjohn, Ph.D.:

Yeah. Makes sense.

Dr. Joseph Mercola:

So, the other thing would be endotoxin as a result of an imbalanced microbiome. So, typically you have a certain type of gram-negative. It's typically pathogenic bacteria that develop as a result of damage to the body from a poor diet. And they get this imbalance, too many of those pathogenic gram-negatives as opposed to the beneficial, things like akkermansia, which is also gram-negative, but makes no endotoxin, no endotoxin. So, I think it has to do with, it's totally related. See, the gram-negatives that produce endotoxins are facultative anaerobes. In other words, they can metabolize oxygen and still survive. The obligate anaerobes, like akkermansia, they get a few molecules of oxygen, they are dead. Dead as a doorknob. So, it's this shift of increasing the oxygen tensions in the colon that causes this transition.

And the reason I'm mentioning that [is] because most people have that. That's what they have. They don't have – I'm looking at a really careful stool analysis for some work that we're doing on using CO2 insufflation to monitor the concentration of these organisms. And one of the most popular tests out there, I think it's BioDiagnostic Lab. They have one-third of the people they're testing, one-third, no akkermansia. It's undetectable in the colon. Undetectable. And it's supposed

to be 10%. 10% to zero, that's a common problem. So, the reason I'm mentioning this, because I'm not sure if you've bumped up against this in your analysis, or if you're focusing on that at all, but the clinical complication of that, if you have a disrupted microbiome and you attempt to eat foods that would have fibers that don't digest very well, you run into problems because you don't have the microbiological capacity to ferment those properly. And even if it does, it's not there.

And those facultative anaerobes are going to consume it, and it just creates this domino series of disasters. So, it limits you from eating healthy foods without negative consequences, serious negative consequences, like producing a lot of endotoxin. So, I'm wondering what your experience with that dilemma is?

Chris Masterjohn, Ph.D.:

Well, I am certainly not as down the rabbit hole of the microbiome as you are. The reason for that is, I view the microbiome as high-level epiphenomenon of multiple layers underneath that I don't think get the right attention by the functional medicine microbiome-centric crowd. So, I think a lot of people are very focused on what substrates feed what gut bacteria, and I think about it like this: So, at the very base layer, what you need is optimal energy investment in creating the landscape of the intestine, which is very complex and sophisticated, and also very precariously determined by energy status. So, if you look at something like niacin deficiency, where they say there's 3Ds or 4Ds, if they're pessimistic enough to include death, the diarrhea of that actually is villous atrophy that looks just like celiac disease.

And the mechanism is that because your small intestine is assaulted by everything in your environment in a way that inside your body is not, the mouth and the anus is outside the body, all the selection of what should come in and what doesn't come in is not protecting the small intestinal cells, they are the ones doing that. And so, because they're assaulted by everything in the environment every day, they have a life of three to four days, and then they sloth off into the feces, and you make new cells that migrate up. Making new cells, it requires a lot of energy-

Dr. Joseph Mercola:

A lot of energy.

Chris Masterjohn, Ph.D.:

So, if you're niacin-deficient – and this is just one example of many reasons you would not have enough energy. If you're niacin-deficient, you get diarrhea because you can't make those cells anymore and the villi flattened, just like they do in the autoimmune attack posed by celiac disease. And so, that's just an example of how energy intensive it is to maintain that infrastructure. Anything that's on that is very much determined by whether it is there, right? Like we were talking about building the foundation of the house before, if you're talking about the microbiome, this is about picking out the right lot of land, and make sure that someone groomed it before they decide to build a house there.

Then, on top of that, you have endogenous secretions of, for example, mucin films. And as much as practitioners are often trying to break biofilms, your mucus layer makes a natural biofilm, and

there's bacteria that are inside it, and they're not even on the surface. And your immune function, which is also very energy-intensive, is then regulating your microbiome. And then I think then after that, what you're eating and whether it's feeding this or that comes into play. So, absolutely the microbiome is super important-

Dr. Joseph Mercola:

Well, let me-

Chris Masterjohn, Ph.D.:

I think sometimes we lose sight of the-

Dr. Joseph Mercola:

Let me tie it up for you, because I think you may have some really, really good points. It reminded me that the reason that you have the microbiome disruption, one of the fundamental reasons, is mitochondrial dysfunction. And I don't think we have a disagreement there. You are unable to produce high-efficiency cellular energy, you just can't do it, for a variety of reasons. And I think one of the biggest is metabolic poisoning with linoleic acid. So, you get this disruption. And the akkermansia I referred to, I don't know if you know that the species name is muciniphila. It is the primary species that makes mucin in the gut. And the reason I had mentioned before the bone broth, because it was tied into this. Because if you have a disrupted microbiome, absolutely akkermansia is going to be [inaudible 01:13:37], as it isn't in a third of the people that the company's testing. A third. It's not there.

So, one of the strategies they can use, and why I think [Dr.] McBride's – [Dr.] Natasha Campbell-McBride, crazy long name – but that's why one of the things was her program worked, and I didn't realize at the time, 15 years ago, is that it's restoring. It's sort of a Band-Aid for the gut lining, until you are able to get things flowing. That's why I was thinking – And just recently, I was thinking about this this morning, because I had a friend give me a complex pediatric case to review, and it was clearly gut dysbiosis. And I recommend, as part of the strategy, bone broth, and I think that's going to be a really effective strategy. And you're a smart guy, I just was wondering, in light of all those things – it seems to make sense, it's like a Band-Aid for the gut, in addition to all the beneficial nutrients. It's magnificent. And most people, especially people who are eating meat, are not getting enough collagen. They just aren't. So, in light of that, what do you think of that strategy now?

Chris Masterjohn, Ph.D.:

Of the GAPS diet?

Dr. Joseph Mercola:

Well, no, the whole thing. Yeah, just using bone broth in that scenario, considering it's just pervasive. I don't think it's widely appreciated how damaging that is. And there's trillions of these things, we have more mitochondria than bacteria, mostly in our large intestine.

Chris Masterjohn, Ph.D.:

Yeah-

Dr. Joseph Mercola:

It's really an organ. It's really an organ. You can make a good argument for that. It's not endogenous, they're different than us, but it's still, it functions like an organ. Because they make all these peptides that – They've got this drug, these Wegovy and Ozempic, that are GLP-1 agonists, that literally all they do is make what akkermansia makes, except that akkermansia does it better because it's pulsatile and not chronic. But they make a lot of other peptides, they make [inaudible 01:15:36] acids. There's an unbelievable interaction, interplay and synergy with health and optimizing that. I dismissed it before, but I'm coming around, and thinking this is where the focus is. If you don't have a healthy gut, it just doesn't work.

Chris Masterjohn, Ph.D.:

So, I think that there's certainly a problem where if you can't eat healthy foods because of the way that they're causing gut dysfunction, et cetera, but I've seen some amazing cases where someone has small intestinal bacterial overgrowth and then they supplement with high-dose thiamine and it just disappears.

Dr. Joseph Mercola:

Really? That's interesting.

Chris Masterjohn, Ph.D.:

And so, I think that example is a case where they stumbled into it by luck, but they fixed a major reason for their own idiosyncratic mitochondrial dysfunction. And then that became apparent as the dominant driver of the microbiome.

Dr. Joseph Mercola:

So, that's a good argument for your original discussion, which was these individual variations that address the fundamental reasons why you might be having these issues, because it results in potentially nearly catastrophic destruction of your physiology.

Chris Masterjohn, Ph.D.:

Yeah. And I'll just also say that before I was talking about how, generally, if I feed Complex II versus Complex I, my lactate goes down, my health goes up. One of the things that happens when I really know I'm optimizing around that is: (a) I effortlessly lose body fat at a very high caloric intake, and (b) I start having two super, super perfect bowel movements a day. And so, I think it's – The issue is how fast can you figure out the idiosyncratic bottleneck and fix it? And does it require – Does it or does it not have a conflict with the damage that's done to your gut? So, for example, if you really should be on a high-starch diet for some reason, but now you've

wrecked your microbiome such that eating a high-starch diet feeds the wrong things, then you might have some chicken and egg type of stuff to figure out, what's the best strategy for that.

And then, there might be other times where it's like, literally all you need is 2,000 milligrams of thiamine, and it's like a miracle, and you don't really have that conflict. And then, of course, there's all kinds of permutations of gray areas in between those two polarities. So, I do think it makes sense to – Basically, what I would do is, I would be trying to look for and fix the underlying cause at the most – Providing that you're also doing the low-hanging fruit as tolerated by the current situation. I'd be trying to find and fix the underlying bottleneck, and then I would be borrowing from the basic principles of GAPS diet, bone broth, et cetera, on an as needed basis, to try to make sure that you're not eating foods that are irritating, and you are eating foods that are healing for the gut. I do think glutamine has a particularly significant role in gut healing as well, alongside glycine and bone broth.

Dr. Joseph Mercola:

I think glutamine is in bone broth, I'm pretty sure. It's a pretty high concentration.

Chris Masterjohn, Ph.D.:

Yeah. Let me – I actually have a spreadsheet with that. So, the glutamine in gelatin is – It's in there, but it’s 2.58% of the protein, so it's not super high. What is very high in glutamine as a whole food is chicken drumsticks and pork hind shanks.

Dr. Joseph Mercola:

Two foods I wouldn't recommend. Unless you raise those animals yourself. And I do raise my own chickens, which is why-

Chris Masterjohn, Ph.D.:

That's the thing, you got to get low-PUFA pork hind shank.

Dr. Joseph Mercola:

Which is why I have a livestock guard dog, who takes the predators.

Chris Masterjohn, Ph.D.:

Aw.

Dr. Joseph Mercola:

My puppy.

Chris Masterjohn, Ph.D.:

But she kills predators.

Dr. Joseph Mercola:

But she kills predators. She kills predators. If you raise chickens, you got to have something that kills predators because I've had more than 50 chickens killed.

Chris Masterjohn, Ph.D.:

Yeah, your pigs will eat them, right? If you have pigs, too.

Dr. Joseph Mercola:

Oh, I don't have pigs, I don't live in a farm. I would not have – I live in a residential area.

Chris Masterjohn, Ph.D.:

Well, I've talked to people who owned both, and their pigs eat their chickens.

Dr. Joseph Mercola:

Geez. Yeah, I'm not a big pig man. But chicken eggs are some of the healthiest – What do you perceive as the healthiest foods? I think it's chicken egg yolks and liver. Probably the two most densely useful foods on the planet. What's your vote?

Chris Masterjohn, Ph.D.:

So, I think the foods that would be most helpful in hitting all your nutrient targets would be egg yolks, liver, like you said. Oysters.

Dr. Joseph Mercola:

Yeah, oysters. Yeah.

Chris Masterjohn, Ph.D.:

I'd make an argument for maybe splitting oysters and clams. And unfortified nutritional yeast would be up there. If you hit those, you're pretty much hitting everything, but you are kind of missing some plant-centric nutrients like vitamin C. I think bell peppers are super useful as a – especially the lighter colored ones, yellow, orange and red. Out of the foods that are in a standard grocery market in the Western world, those have the highest vitamin C-to-carbohydrate ratio-

Dr. Joseph Mercola:

Oh, come on. You're missing the biggest one, and you live in Florida, and you can get them. Acerola cherries.

Chris Masterjohn, Ph.D.:

Well, that's why I put the limitation of, that you would go to the grocery market-

Dr. Joseph Mercola:

[inaudible 01:22:23]. But you can grow them where you're at.

Chris Masterjohn, Ph.D.:

I'm saying out of the standard – I'm not saying the most esoteric superfood, I'm saying the most standard, run-of-the-mill, everyone – Out of the things that people normally eat, I think bell peppers are very useful as a [inaudible 01:22:40].

Dr. Joseph Mercola:

That's for sure. But living in Florida, we can have acerola cherries, almost year-round.

Chris Masterjohn, Ph.D.:

Do they have them at the grocery store? I haven't seen them.

Dr. Joseph Mercola:

No, you have them in your backyard, when you grow them.

Chris Masterjohn, Ph.D.:

At the farmers market, yeah.

Dr. Joseph Mercola:

I've never seen them in a farmers market. I've only seen them in – You have to have your own tree. Because they're very perishable, they don't last too long.

Chris Masterjohn, Ph.D.:

I don't have a backyard. I'm in Miami. [inaudible 01:23:06] backyard in Miami, but-

Dr. Joseph Mercola:

Hey, I'm going to be your neighbor, I'm moving down there. Yeah.

Chris Masterjohn, Ph.D.:

Oh yeah?

Dr. Joseph Mercola:

Yeah.

Chris Masterjohn, Ph.D.:

Cool. When?

Dr. Joseph Mercola:

Later this year. I'm going to enjoy the summer where I'm at now.

Chris Masterjohn, Ph.D.:

You're not going to hate the population density?

Dr. Joseph Mercola:

I will hate the population density, it's lesser of two evils that I have to contend with. I'm not going to drive in Miami, that's for sure.

Chris Masterjohn, Ph.D.:

Yeah, I don't drive much.

Dr. Joseph Mercola:

It's almost as bad as New York.

Chris Masterjohn, Ph.D.:

[inaudible 01:23:33].

Dr. Joseph Mercola:

So, we'll have to hang out when I get down there. All right.

Chris Masterjohn, Ph.D.:

Yeah, sounds cool.

Dr. Joseph Mercola:

So, any other things you want to close on? Why don't you tell us your site, and things like that?

Chris Masterjohn, Ph.D.:

Yeah, go forth and do the low-hanging fruit, and then when you really want to optimize the next thing, after you've really got that all on lock, I think that's where it's time for some self-experimentation, and it really helps to know a little bit about biochemistry, and do some testing like glucose, ketones, lactate, or some tracking micronutrients in Cronometer and so on. My website is chrismasterjohnphd.substack.com, and if you subscribe to my newsletter, I talk about this stuff all the time. So, if you ever want to jump down the optimization rabbit hole with me, my newsletter is where to start that.

Dr. Joseph Mercola:

All right. Well, keep up the good work, Chris.

Chris Masterjohn, Ph.D.:

Thank you.

Dr. Joseph Mercola:

How often do you get outside and enjoy that tropical sunshine? Or subtropical sunshine? How often do you do that?

Chris Masterjohn, Ph.D.:

How often do I go outside?

Dr. Joseph Mercola:

And maybe what was your last vitamin D level? I'm assuming you don't swallow vitamin D.

Chris Masterjohn, Ph.D.:

I haven't tracked vitamin – I don't take it because, so when I was in New York, I would always go out at solar noon for 40 minutes with no sunscreen. In Florida, I don't monitor it as much. I have a balcony that all across the day has direct sunshine, so I usually am out there for hours just working in the sun and whatnot. So, I actually haven't tested my vitamin D anytime recently, but I'd be surprised if it wasn't 50 or 60 or something, just because of the sun-

Dr. Joseph Mercola:

I think it's a good marker, it's not just for vitamin D, because if you're not supplementing with vitamin D, then it's a marker for sun exposure.

Chris Masterjohn, Ph.D.:

Yeah, that's true. Although, I get so much sun exposure that I really don't have to go out of my way to optimize that, it's a pretty firm habit for me.

Dr. Joseph Mercola:

For others who aren't, it's an interesting marker.

Chris Masterjohn, Ph.D.:

Oh yeah, no, for the average person, they really need to think more about getting outside. Absolutely.

Dr. Joseph Mercola:

To me, it's one of the most fundamental basics, and it doesn't really cost much, except time.

Chris Masterjohn, Ph.D.:

Yeah. No, I agree, getting the sun is – So, morning sun for your circadian rhythm, and afternoon sun for the vitamin D, and other benefits.

Dr. Joseph Mercola:

All right, well, this has been great, you keep up the good work, and enjoy the sunshine.

Chris Masterjohn, Ph.D.:

Thank you. You too.

Dr. Joseph Mercola:

All right.

Chris Masterjohn, Ph.D.:

Thanks for having me.