Basic Blood Chemistry for Better Health Optimization: A Special Interview With Bryan Walsh

By Dr. Joseph Mercola

JM: Dr. Joseph Mercola
BW: Dr. Bryan Walsh

JM: Welcome, everyone. This is Dr. Mercola, helping you take control of your health. Today I'm joined again by Dr. Bryan Walsh, who is going to enlighten us about a number of things, but primarily on some of the amazing pieces of information you can harvest from your blood test. Imagine that. This is information, most likely if you're seeing a conventional physician, he will not tell you, and he probably doesn't even know more than likely. You definitely want to listen to this, because it's going to be fun. Welcome and thank you for joining us.

BW: Thank you so much. I'll even add to that, if you don't mind. I think that there are a lot of functional medicine practitioners, unfortunately, who aren't aware of this information as well. It's not anybody's fault. Just quite frankly, I think rare is it that somebody really digs into some of the scientific literature and pulls out some really useful stuff. I think that in the functional nutritional integrative medicine world, it's high time that we take what we have been doing with blood chemistry to the next level.

JM: Okay. How did you get so smart? How do you know this and they don't?

BW: First of all, I don't think I'm very smart. I honestly think that most of us don't really know as much as we think that we do as a medical industry, even as an alternative medicine industry. But my story – I will tell you in sort of a shortened version – is I graduated from naturopathic school. I was really excited to practice –

JM: Excuse me. Let me interrupt there for a moment, because there are two types of medical doctors (MDs). There are the ones who went to the four-year schools and generate typically a debt of a quarter million dollars by the time they graduate, and then there are the ones who do the night school version.

BW: Or if you end up marrying one of the people in night school, then it's twice as much in debt.

JM: Because your wife's an MD too.

BW: That was the most expensive but best date ever. Yeah. I went to one of the four-year universities. But to be really honest with you, at this point in my career – and I know you can understand and respect this – it really doesn't matter what letters are after my name. Knowing what I know, I could practice as a medical doctor or a physician's assistant, a naturopath or any variety. It's really about the knowledge and not so much about the degree. The degree was just kind of a ticket to be able to play in the game in the first place.

I went into school and I was very excited. I had a long history in health. I was a fitness professional. I was a massage therapist. I did all of these things. I was reading nutrition books even as a teenager. This was kind of a pinnacle for me. I went to school. I sort of had a lackluster education, which I didn't really fully realize until I got into practice.

I had had a course in blood chemistry. It was a very standard course, where you have your Fishbach as the text. It has all the markers. If they're high or they're low, here are all the different various pathologies it could possibly be.

Shortly after I was in practice, I was looking at blood chemistries. If something wasn't outside of the laboratory reference range, I had no comment on it. If things were outside of the laboratory reference range, I had to look them up. It was really frustrating to me. My wife and I looked around. We found a functional blood chemistry weekend. It was put on by a supplement company. We went to it and it was great. It was, at the time, exactly what we were looking for. But then the problem was – there were a few problems.

JM: What was the company? Was it Biotics?

BW: Well, it was Apex. If you know the story, the reference ranges, they promoted these optimal or functional reference ranges, which were originally from Biotics, but there wasn't any scientific validation to these. They sort of came from the ether. When asked, "Where do these ranges come from?" there's never really a solid answer. That didn't really sit well with me. Although I think, the idea of a narrower set of reference ranges makes a lot of sense. Logically, it would be nice to have some sort of science to back that up.

Then the problem was as I was looking at these labs, I realized I have no idea what these markers even are in the first place, I mean what they really are. I'll never forget that the first marker I decided to delve into was albumin. I'm looking at a lab and I thought, "What really is albumin? I mean, what really is the physiological story of albumin? Where is it made? Under what conditions is it made?" The people who had been looking at labs for a while may think that that's easy. But when you don't know what you're doing, it's brand new.

What I found – There are many times in your career where you have sort of those moments, I realized that when I knew the whole physiological back story of albumin, not even as a blood chemistry marker, that I didn't need a book to look up as to why it was high or it was low. When you know the reasons that it's made, where it's made, and why and how it's stored and how long it lasts, its half-life – all these things you can look at in a lab and you can, by yourself, think through why albumin might be high or low.

It was kind of like that movie The Matrix, where I sort of had this taste of what it was like to really fully know a marker. I thought this was well over a decade ago and I haven't stopped. I then realized I need to learn the physiology of every single one of these markers as best as I possibly can. The more that I knew that, the more they started to make sense about labs.

But in so doing, I also came up and found a lot of issues. One, is this ideal of optimal or functional reference ranges, which we can talk about. They were sort of arbitrary, but it turns out that there

are a lot of published literature that suggest that an optimal – there's a better reference range for almost every single marker that you could find on the standard blood chemistry.

Here's another story though. This is a real problem. When I originally learned this, I had been taught things like bilirubin – "There's no such thing as a low-end of bilirubin. There's no functional range for a low-end on bilirubin." In fact, it could be 0.1, and that's still okay. But when I started digging into the physiology of these markers myself, I couldn't believe what I was reading. I couldn't believe that men and women should have different ranges for aspartate aminotransferase (AST) and alanine aminotransferase (ALT). It was very clear in the literature that these markers that we're using for fatty liver, like AST and ALT, are horrible at it. They'll never find fatty liver with AST and ALT.

Things like bilirubin, which I was taught is fine if it's low, couldn't be further from the truth. Bilirubin – we can talk more about this if you want – But low bilirubin is very clearly associated with an increase in all-cause mortality. Then the question is, "Why?" Then you learn bilirubin is a lipophilic antioxidant. It's a marker of lipid peroxidation, which you know at this point – but go backwards.

JM: This is total bilirubin.

BW: Total bilirubin. Right, right, right. Here, we now have this marker of lipid peroxidation, essentially, which is an incredible marker to have. That when you look at the literature, you can look at what level might indicate the excess liquid peroxidation is taking place. The question is how many practitioners know that information? I didn't. I had to teach myself this information. How many practitioners, either conventional or otherwise, are not using bilirubin for the marker that it should be?

JM: I'm curious. How did you teach yourself? Since you didn't learn it in a course. I'm assuming you took the tools that you were given during your naturopathic training and your intuitive wisdom. You somehow collated this information. What was your process?

BW: Well, you want to know the truth, I like to do things – I started from scratch. I just cracked open the physiology textbook and I just started going through it again. I had physiology. I had physiology as a prerequisite into the program. I had a couple of semesters of physiology in the program itself. But I also think that – This is a whole other conversation – But the way that things are taught in education today are not very conducive for retention, for learning and for understanding and putting things into context, so that you can understand these things later.

Like with biochemistry, you can teach glycolysis. You can have students memorize all the 10 enzymes. But then, what's the context of that? What's the context when it comes to glucose regulation, insulin resistance or the offshoot of pentose phosphate pathway, and how those might interact in some ways. There's no context. I think that's why I didn't really learn. I didn't understand. I didn't fully get these things.

I just started with some physiology textbooks. I just read chapter 1 and went through the whole thing. When I did that, I went back and I did it again. The second time I learned more than I did

the first time, because I had a better foundation. I haven't stopped, quite honestly. I think I've graduated from most physiology textbooks –

JM: And now you're pursuing the literature.

BW: The literature is the best place.

JM: If you're just reviewing the literature, boy, they're better than the textbooks. It's state of the art. They have the references. Sometimes it's just a few months old. They can tell you what the state of the knowledge is at that point.

BW: Yeah. Absolutely. I think that the literature is really the only place to go nowadays for myself.

JM: Yeah. Thankfully, we have PubMed. When we both first started, it was very difficult because unless you had academic credentials and you could have access to these articles, you'd have to be independently wealthy to afford looking at them.

BW: Absolutely.

JM: Now a good percentage – Maybe one-third of them are free.

BW: Yeah, yeah. Thank goodness for all the open-sourced ones that are available nowadays. It's certainly helpful, and to be associated with academic institutions is also helpful.

JM: Do you have an association?

BW: Yeah. No. I'm an instructor at the – actually an associate professor at the University of Western States.

JM: Oh. Great. That helps.

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BW: Yeah. No. I don't want to tell too much of my own personal story. But I've wanted to teach – I've had teaching within me for a very long time. I've taught, as a naturopath quite honestly, at the community college level. I've taught at a couple of graduate level courses for different institutions. I think that's something that's actually important. It's one thing to be a clinician. It's another thing to be a teacher. But I think when you do both, if you're a clinician who teaches and you can teach clinical stuff – it's not just theoretical – they really feed into each other. It's something that I've always enjoyed.

JM: Teaching your passion – we may want to take a small tangent now and go back to it later – But one of the reasons we're doing this interview is that you are actually going on a tour, not only by yourself, but with your wife and your children. You've got a new motorhome and you're traveling around the entire country. You're going to be teaching people. Why don't you tell us a little bit more about that?

BW: Yeah. Thanks for that. Yeah. I'm not sure how the idea came about, which is probably a good thing. I don't know if it's passion. I don't know if it's crazy or if it's ambitious. I'm not sure what it is. But we're taking – We have five children, aged 10 and below: 10, 8, 6, 4 and 2. And a dog, and my wife. We're packing it up. We're going in a recreational vehicle (RV). We're spending basically March through October hitting almost 30 different cities throughout the U.S. to deliver a weekend workshop or seminar, put on by myself, in the areas of functional medicine and blood chemistry interpretation.

I've talked to you about detox and some of my thoughts and programs on detox. I'm going to be putting some of that in there. I have some work that I've done on glucose regulation. I'm just really trying to take the best of what I've learned in functional medicine, more so in blood chemistry interpretation, and packing in a whole weekend of that. I actually should add, because this is the educator in me, I haven't seen a weekend seminar that's ever done this. I mean this is – This is, by the way, just totally us. It's not sponsored by anything.

JM: Yeah, yeah, yeah.

BW: Totally us. I've actually added to this to make sure that people get the most information they possibly can. When people purchase tickets, they get access to five hours of video, whiteboard video, where I teach the physiology of the markers in the first place. So that if somebody is a seasoned veteran and hasn't had physiology for a long time or if someone maybe didn't get as much physiology as they needed to, when everybody goes into the weekend at a given city, they've all watched the same videos, and maybe even rewatched them.

I don't go into the highs or the lows of the different markers. I just teach the physiology, so that when we hit the 16 hours for the weekend, everybody's on the same page, and we can just hit the ground running and really start talking about content. I'm really excited about it.

JM: Yeah. So am I. I'm actually going to one. The one that's closest to me is in Jacksonville, Florida. I'll be attending that one also. Just to share my own personal experience on learning postgraduate. I mean the stuff you're teaching is not taught in any medical school. Very similar to my process after I graduated medical school was like 10 years later, I started to appreciate natural medicine and really focused my direction towards that area.

The way I learned it was to go into these types of educational events. There are two types. One where a number of different speakers present, it might have been 10 to 20 speakers over the weekend, and one where it's just one. I found, personally, that the one where there's only one individual. You can really, really learn. Not that you can't learn from the other one, but what can you teach someone in an hour when you have a large depth of knowledge to share? It's almost impossible. That's why I get somewhat frustrated. If someone gives me 10 minutes to speak or 20 minutes, I mean what are you going to tell them? It's really restrictive.

I'm really excited to be attending your event and learning more about this topic. I would encourage anyone who's a healthcare clinician to attend one of these in the 30 cities that you're going to be presenting at.

BW: Yeah. I'll just piggy back on that. I totally agree. When you're doing it yourself, and I'll just go ahead and say it again, it's not sponsored. I've been to seminars, where it's sponsored by a lab or it's sponsored by a supplement company. It's just the nature of what it is. The studies that they will show you are biased in order to help promote whatever it is that they're selling. They tend to leave out the other ones. Information has been inaccurate when I've gone to some of these things before.

It's literally just me and my family. We'll see what happens. We were joking around about having the kids and my wife will have the same shirt. Because they're going to be taking tickets. They're little, but why not, let's get them to work and make sure people's waters are filled or whatever it might be. The 10-year-old's kind of like this real crazy tech kid. He might be the audiovisual (AV) guy. I have no idea yet. We haven't done this thing yet.

But that's why I added those five hours of video first. It's so that we can just jump right in and talk deeply about this stuff. So people go away at the end for whatever the price of the ticket was. They might use this stuff for 10 years. They may have the references and the materials that they can use for so long that they actually learn something. That it's not just watered-down, sexy-sounding, cool, sound bites. Instead, it's actually useable information.

JM: That's really great. Why don't you share with us some of the highlights of what you're going to be presenting. You've given us a few examples. But maybe you can share a few more, even go deep on and give people a taste of what it's going to be like.

BW: Yeah, yeah, yeah. One of the things – I guess I could share my screen, but I actually don't know where this little graphic is right now. But what I did is I created an infographic. I basically call it the cellular theory of health.

The foundation of this, going back to basic physiology, is – you're familiar with the levels of structural organization, and time formatting, which I think we have – I'll just go through this really quickly. You remember that the levels of structural organization, as taught in a physiology course, it's usually in chapter 1 of every physiology text, but nobody pays attention to this.

I remember it was years ago. I was looking at this and I thought, "There's really some wisdom in this." The levels of structural organization basically answers the question, what we're made up of on a physical level. On the smallest most microscopic level, that cannot be further separated in nature, we're made up of atoms, chemicals or elements, things found off the periodic table – carbon, oxygen, nitrogen, phosphorus, calcium, magnesium, molybdenum, all those things. Then if you take two or more atoms, chemicals, elements and put them together, then you get – I could quiz you on this if you want – then you get a molecule. People think of things like water, but glucose is a molecule. Amino acid is a molecule. Triacylglycerol is a molecule.

JM: The smallest molecule in the universe, hydrogen.

BW: Right. Molecular hydrogen.

JM: Yeah.

BW: Not atomic. Right.

JM: Right.

BW: Then you take molecules and you put them together, then you can get a macromolecule. If you take a bunch of glucose together, you can get glycogen. You put a bunch of amino acids, you get a protein. You put a bunch of – I always say, "Three triacylglycerol is a glycerol molecule. You get a triglyceride," for example. I'm sorry. "Three fatty acids and a glycerol, and you get triacylglycerol."

Then if you take these macromolecules and put those together, then you make organelles. That's all the parts of a cell that we always talk about – the mitochondria, the endoplasmic reticulum, the ribosomes and the nucleus. Then if you take those and you wrap them in a phospholipid membrane, then you get what's called a cell.

This is the first part, so far, that's fully capable of life, when you think about it. I'll take the levels of structural organization on, and then I'll come back to this cell in just a second. Then if you take a bunch of cells and put them together, you get tissues. There are always four different types of tissues in the body. There are connective, neural, muscular tissue and epithelial tissue. If you take the four tissues of the body and put them together, you get an organ. The stomach has all four. The heart has all four. Most organs have all four to some degree.

Then if you take organs that have a similar function, you put those together, you get an organ system, like the digestive system and the respiratory system, the integumentary system. Then if you take all the systems, then you get an organism. I'll take this further on the weekend. But you also have communities and populations.

Now, here's the whole point, and I'll go into this. I'll share the infographic I have in just a second. It's the foundation of the whole weekend, but I talk about blood chemistry the majority of the time. Think about this for a second. When somebody has a sign or a symptom of any kind, like the organism has a sign or a symptom, then you go backwards in the levels of organization.

Let's say they have premenstrual syndrome (PMS) or there are issues with infertility. In those cases, it's not the whole organism. It's an organ system. What would it probably be? It would probably go towards the endocrine system, right? But an organ system is really made up of a bunch of organs. In a woman who has PMS, it's probably not her thymus. It's probably not directly her adrenals or pancreas. Well, go ahead and say it's probably your ovaries.

According to levels of organization, an organ is really four different types of tissues. So then, if this woman who's suffering with something, what's dysfunctional? Is it the epithelial cells? Probably. Because those are the hormone-making cells of the ovaries. It's not the connective tissue. It's not the muscular tissue of the ovaries. It's not the neural tissue probably. But epithelial tissue is really just a bunch of cells. Really then, where is the dysfunction in this woman coming from in the first place? It's the cells.

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To put it in another way, healthy cells make healthy tissues. Healthy tissues make healthy organs. Healthy organs make healthy organ systems. Healthy organ systems makes a healthy organism. I've created this model. One could argue about healthy organelles, like the mitochondria and the endoplasmic reticulum, but if you have healthy cells, then you're going to have a healthy organism, because cells make tissues make organs make organ systems make the organism.

Let me try to share this infographic with you really quickly if I can. This is the foundation of the whole weekend, because what this basically is is that when you think about, "What do cells need?" They need three things. One is they need to be able to make energy. Actually if I get really fancy – Well, I don't know. When's the last time you've had someone get fancy like this?

JM: You're going to paint right on the screen. Alright. Great.

BW: Over in this area here, the cells need something. They need to be able to make energy. To make energy, they need oxygen. I'm not going to go into details right now. But they need oxygen for the electron transport chain. They need the right substrate, glucose and fatty acids. They have to have healthy organelles. They have to have the right micronutrients in order to be able to run all these biochemical processes inside the cell. If one of those things is dysfunctional, you have a dysfunctional cell, then you have dysfunctional tissues, dysfunctional organs, organ systems and organism.

Let's say all this is good. The second thing you need is they need to be protected from things that could otherwise damage them. Let's say everything over here is good, but over in this next area, infections can cause cellular dysfunction. It is an immune system dysregulation. Here's an antibody that can cause cellular dysfunction. You have reactive oxygen species here. Here's another one. I'm blocking the last one. I can't really circle it very well, or toxins of some kind.

You can have all the nutrients, all the substrates, all the fatty acids, metabolic flexibility, the micronutrients that you need. But if you have toxin exposure, reactive oxygen species, immune system dysregulation or infections, then you'll cause cell dysfunction. Again, cell dysfunction, tissue dysfunction, organ, organ system and organism dysfunction.

Let's say both of these are doing alright. Then you have, down here, is it has to be the right environment. The pH of the cell has to be good. The hydration status has to be good. A couple of topics that I'm really excited to go into is cell communication. If a cell can't communicate with another cell then it basically doesn't exist. Similar to us and those studies on infants, for example, if they're not communicating or interacting, then they don't develop.

And then here is – this is a little bit more esoteric, but the papers on this are pretty awesome – community. One cell in isolation in our body is not going to do very well. It is a community of cells, and then you extrapolate that to all the papers that are done on purpose, loneliness, connectedness and all of those types of things. It's an area that I'll get into as well.

Then the last bit is that your genetics, your epigenetics, can influence all of these things. That's the foundation of the weekend. Then what I do is I'm going to go into how you can evaluate most

of those components using a blood chemistry. The reason why is, as you know, a blood chemistry, one of the areas that I think that we really messed up in the alternative medicine space is we don't pay enough attention to this scientifically validated, internationally respected, the most accurate of any lab, inexpensive lab test as a blood chemistry.

We instead jump to these really expensive, fancy with beautiful, colorful PDF reports. Nothing can tell us even close to what a blood chemistry can tell us if we know what we're looking at. In terms of highlights when we talk about the blood chemistry, I have, over the years, compiled – I don't know how many papers now – well over 100 papers that have optimal reference ranges easily for most of the majority of the major markers found on a blood chemistry, even some ancillary ones, like A1C and some other types of markers. The value of that is tremendous.

What that means in English is there is the laboratory reference range that we as practitioners rely upon. But it turns out that there is an evidence-based set of optimal reference ranges, that if you look hard enough from the literature, that are better at predicting, so that something is abnormal, then the laboratory reference range is provided. Glucose, for example, all the studies that I've looked at –

JM: This is one you could do at home.

BW: Yeah. The glucose – That's great. There's a great study looking at postprandial glucose levels, so elegantly done. But basically, I am of the opinion that fasting glucose should be anywhere between 82 to 88. That's based upon four or five studies that I've looked at, also with physiology.

I know that people debate this and say, "Well, 75 is healthier," or whatever it might be. And I've looked at it a lot. You have to consider the physiology for example. "When does glucagon kick in? When does insulin start to shut down?" Because if we look at what the body would do normally, we have to take that into consideration and then add upon that some other papers that I've looked at. I guess people don't have to go on. That's just based on all the papers that I've read about, that 82 to 88 is a pretty solid glucose fasting.

In terms of non-fasting, which basically means that somebody should take a glucometer at any point of the day, even if they just ate. I don't care if it was an hour ago or two hours ago, or even 15 minutes ago and should be anywhere between about 82, since that's the low-end, and about 130, based on this one really elegantly done paper that I'll show during the weekend that was done on a couple of different meal types postprandially, and they follow continuous glucose, and to see how high glucose –

But the inclusion criteria in the people in the study is phenomenal. They were super healthy. That's one example. I'll go through all the different reference ranges, optimal reference ranges and show you the papers that they came from and why I came up with the conclusions that I did. Here's an example. AST and ALT, what's the lab range for that typically? The upper end since last time you looked at a lab?

JM: It's 100 something.

BW: It's usually 40 to 50, I think, in terms of a standard lab.

JM: Okay.

BW: But the papers that I've looked at very clearly show that, A, men and women should have a different AST and ALT reference range, very, very clearly. B, it's not much above 20. Here, these labs are reporting 40 or 50 as an upper end, but there are multiple papers that say that an AST and/or ALT and gamma-glutamyl transferase (GGT) shouldn't really be much above 20.

When they start to go above 20, but they're lower than 40 or 50, nobody's calling them out on that. GGT, we talked about that before. I know you've had some people on talking about GGT. GGT very clearly, there's been meta-analysis done on these with over 600,000 people included entirely. They'll say things like, "GGT, in the physiologic range, is an increased risk of all-cause mortality."

What that means is high-normal. Below the laboratory reference range, you still have an increase in all-cause mortality. If your GGT is a little bit high. We need to modify that reference range. How many doctors are looking at GGT and saying it's okay when, in fact, according to the literature, it's absolutely not. The same is true for phosphorus, calcium and bicarbonate. Like I said, I've looked up and spent a lot of time looking at reference ranges for all these things.

JM: Can we tangent to iron for a bit? Because one of the reasons I initially delved into GGT was its influence on iron. Excessive iron will tend to raise GGT. It's another marker, other than ferritin. It's my perception that – I'd be interested in your input on this too, but I believe that the lack of appreciation of measuring iron is probably one of the biggest faults of conventional medicine, because that's such a massive risk factor for disease – cancer, heart disease, Alzheimer's.

BW: Yeah. It is. I would be curious to see the papers that showed that GGT was a marker of iron.

JM: Yeah. I did a whole interview on it.

BW: I only say that because my understanding is that elevated GGT – so there's a few pieces of this – elevated GGT – There's a paper done in 2012 that showed that the red blood cell, erythrocyte, membrane is a target for GGT. When GGT as an enzyme – it doesn't attack it but – modifies the erythrocyte or red blood cell membrane. Then some of these elements, like iron, for example, can become more liberated. When GGT is elevated in the presence of iron or copper, by the way – and that's super clear. They do the same thing.

That because of that – it's called a cysteinylglycine – is liberated from glutathione via GGT. That, in the presence of iron or copper, initiates the Fenton reaction. That's when you get massive oxidative stress. One thing I haven't been able to fully figure out is that if GGT, if iron and copper are more normal, is less of an issue, I still think it's a marker of xenobiotic exposure and of hepatocellular glutathione deficiency, which is a really awesome marker to have, oxidative stress essentially, but most likely, oxidative stress due to glutathione deficiency.

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JM: It's a very inexpensive test.

BW: It should be on every single lab.

JM: Yeah.

BW: I don't know if it's – I have not seen that it's a marker of excess iron. But when GGT is elevated and iron or copper, and I would add to what you said about copper not being evaluated more often. Copper and iron are equally as – toxic is the wrong word – but damaging in the fact that they can cause so much oxidative stress via primarily the Fenton reaction.

JM: We use total iron binding capacity (TIBC), total iron count, to evaluate iron, but what are you evaluating for copper? Ceruloplasma?

BW: Yup. That's the primary one. It seems to be the most accurate one for now.

JM: What are your ranges on that?

BW: I haven't found. That's what I haven't found. I'll tell you. Here's how I come about in many of the optimal reference ranges. It was funny and a little ignorant of me, I suppose. I wanted to validate the optimal reference ranges. I wasn't happy with these sort of obscure ranges that people just kind of come out of the ether somewhere.

Naively, I started looking into the literature to look for researchers who were having conversations about improved reference ranges. That may be that, "The reference range we're not using is not adequate, so let's talk about a better one." They're not having that conversation. They're more interested in disease. I was really frustrated because I was trying to look for these optimal reference ranges for things like albumin or things like ferritin or any of these things.

But then it was by accident. I stumbled across a paper that was looking at – considering in many cases – a U-shaped curve in a lot of these markers and mortality. I thought, well, I don't want that, because I'm interested in optimal health. Mortality is just so gross and it's so depressing. It's on the opposite end of what it is that I have.

JM: It's so inevitable.

BW: Yeah. You're right. But then I was like, "No. I want optimal. I want researchers who are talking about a healthy reference range." But then when I started looking at this, it was really interesting. I thought, "Well, what is the antithesis of optimal health? Of mortality? It's death." When I looked at the ranges that many of these papers we're talking about, it was a tighter set of reference ranges that was offered by the lab. It basically said, "Choose the marker." It could be phosphorus, bicarbonate or even chloride, any of these things that people waste their time on. It doesn't matter.

All across the board, the reference range is generally tighter than what's offered by any of the major labs. What it clearly showed in fairly large population studies that were tracked over a long

period of time, is that you had an increased risk of mortality if fill-in-the-marker was above or below the certain range. I thought, "Alright." Here I was after this optimal reference range, this healthy reference range, but in reading these papers, I thought, "Well, if my phosphorus or chloride, or whatever was out of this range, that's indicating that I have a higher risk of death." Therefore, being within that range is good.

That's where a lot of these ranges came from in the first place. I go back to ceruloplasmin. I haven't really found much. I am constantly looking for studies on finding more optimal reference ranges in health. But it's used as a reference range for that.

JM: Let's go back to iron then. Share with us your analysis of the iron literature and what your perception of the ideal reference changes are.

BW: You chose a hard one.

JM: Why not? You're the expert here.

BW: No, no, no. Iron's been tough. First of all, for men and women – Okay. Look. Actually, say this. The reason why I said the thing about mortality is because you have to look at the enzymes that you're really most interested in. Let's take a quick tangent and then we'll go back to iron.

Let's say for example, you wanted to find an optimal reference range for A1C. Your endpoint was diabetes. There are papers on this. There's no low-end for A1C when it comes to your risk of diabetes. The lower your A1C, the lower your risk for diabetes. Therefore, one could make the conjecture that there's no such thing as an A1C that's too low. But then if you switch your endpoint to cardiovascular disease or cancer or all-cause mortality, then all of a sudden there's a low end for hemoglobin A1C.

You need to be careful of the endpoint. I say that because – I say this all by recollection – there was a paper on iron. I think it was only on men. The endpoint was colorectal cancer. I think they were looking, if I remember correctly, at ferritin levels. That's legit. Where is the guy going to lose his iron? If it's from a bleeding situation, it's going to be a gastrointestinal bleed, since hopefully he doesn't have a menstrual cycle. But that was the only type of cancer, I think. I would have to look back on that study that they looked at.

But for both men and women, it seems that the lower end – I'll even tell you, my slides for this during the weekend have a couple of question marks, because there is some grey area of interpretation of all the differences. But the low-end of ferritin, I think, for men and women should be around 50. In women, I think it's a little bit more, clearly around 115. Men is a little bit trickier. I think men, there are some papers that suggest as high as 200 is okay. But I would tend to err more around 150 in terms of ferritin.

Serum iron levels – My problem with serum iron happened really early in practice. I saw somebody who had a serum iron level that was way above the laboratory reference range initially. So much so that I had her run additional markers, an iron study panel. Then just a few days later, her serum iron had come down to a very healthy normal ferritin reference range. I'd love to hear your

feedback on serum iron. I have found it to be relatively, which is why I tend to use ferritin and TIBC a little bit more.

JM: I think it's important. But I've reached a different conclusion. It may need a more careful analysis of the literature. But for all-cause mortality, assuming that you don't have a bleed, which is going to cause premature – artificially low ferritin levels, I think it should be somewhere between 30 or 40, at least for men.

BW: Ferritin?

JM: Yeah. Ferritin. That's my belief. I could be wrong, but you need iron. Obviously, it's in all the cytochromes. It's in your red blood cells. It's essential for life. If you don't have it, you're going to die. But if you have too much, it's going to cause excessive oxidation. The key is to find balance. I think 80 to 90 percent of the population of adult men and post-menopausal women have levels over 100, some quite significantly more. Maybe a quarter to a third are seriously elevated. Fortunately, it's one of those things we don't need to supplement for. The therapeutic intervention is pretty straightforward. Just give away some blood.

BW: Yup. Yeah. No. Like I said on that one slide where I have some question marks on that, one could make an argument that ferritin should be lower than 100 in both men and women.

JM: Yeah.

BW: In the low end, like I said, in what I've looked at – The optimal is around 50 for men and women. But then at the same time, I think that's a good conversation. It's the value of ferritin, as well as looking at other things, like TIBC, or I think that's more valuable than transferrin. There's a transferrin receptor that can be tested as well. I think that what we're doing is not doing a good enough job of evaluating all the markers related to iron.

It's difficult to just make a statement about "Ferritin must be higher or above or below," because TIBC will really tell you a lot about what the body is interested in. Then there's the bit about, "What form is iron even in in the first place? Is it in a bindable, transportable form that can be used for heme? Or is the role of copper is to make iron more usable?" You have a lot of iron. In fact, I had a patient recently. You have a lot of iron, but your body can't use it or isn't in a useable, storable form, therefore may not be as potentially as damaging. I think that there's more to the iron story for sure. You really have to take a better look at it.

JM: Yeah. It's just something that's rarely screened. I mean the less a person goes in with anemia, even then you can have complications. I happen to have beta thalassemia, which is genetic anemia, somewhat similar to sickle cell. For those of us who have it – typically of Mediterranean origin – they're regularly – I would say probably most likely the majority of the time – are misdiagnosed as iron deficiency anemia.

BW: Absolutely.

JM: They're given iron as a supplement. It's just outrageous.

[-----40:00-----]

BW: One of the things that I'll teach during the weekend is copper deficiency anemia for that very reason.

JM: Interesting. But we don't know the copper agents.

BW: Yeah. There are some insights that one can get. Copper – I don't know how deep you want to go into this. Copper deficiency anemia looks identical to iron deficiency anemia.

JM: Interesting.

BW: Even things like ferritin, iron and TIBC. The reason why is because one of the roles of copper is to turn iron into the form that's transportable and useable in synthesis. Without copper, the body has iron, but it can't use it. The body and its wisdom knows that it can't use it, so things like TIBC will go up because it's looking for iron. Even though it's there, it's not the useable form of iron or the transportable form of iron by transferrin. Copper deficiency anemia on a blood chemistry look identical to an iron deficiency anemia, every single marker.

One marker that can be different is neutrophil. Neutrophils tend to be low when there's copper deficiency. There are so many things that could influence neutrophil. One tip off for someone is it's an iron deficiency anemia that's not being corrected by giving iron. "I've had iron deficiency anemia. I take iron, I eat red meat, I take spinach, I take vitamin C with spinach, and nothing changes." In that situation, one wants to consider a copper deficiency at the same time.

JM: I've got a question on the copper. Does the copper reduce the iron? If so, does it do it directly or does it do it through the intermediate as an enzyme, something like nicotinamide adenine dinucleotide phosphate (NADPH)?

BW: Good question. It does reduce it. I might have to look. I'm 99 percent sure it does it directly.

JM: Okay. That's interesting.

BW: I need to look that up. Don't take my word for that.

JM: Yeah. It's just that these molecules have to collide somehow and share electrolytes.

BW: I mean I say that but the second I say that, it's got to be – It's probably an enzymatic reaction. That's a whole other topic. But we're basically, according to literature, wrong about what antioxidants do. [inaudible 42:28] Vitamin E, definitely, in terms of scavenging. That's the whole argument. I'm not going to get into that now. But that's the whole argument.

It's that here you have these things inside of a cell that are bumping around on each other. That enzymatic reactions are catalyzing these things so fast. That made me naively think that vitamin C is going to get inside of a cell and just – If there's huge party where there's a billion people inside of the room and one person wants a glass of water at one side, you will have that glass of

water on the other side, the chances of you making it to that person and handing them the water is basically not going to happen. Then why do we think that this magic antioxidant with this extra electron will happen to bump into the thing [inaudible 43:13]?

JM: I think that would be true for exogenous antioxidants, ones that are supplemental. But if you hormetically induce your body to make them, then they're targeting and you need them.

BW: Well, getting back to things like bilirubin, uric acid or –

JM: NADPH is my favorite.

BW: Yeah. No. That's a good one. Yeah. The pentose phosphate pathway. Then a couple of other things that I talk about during the weekend was – Another thing that really bugged me is I would look at a blood chemistry and I was positive that there was more information that could be gleaned from it than was actually on the page of that. In terms of calculations, there's got to be calculations or ratios or different things that we could use. I'm sure you're probably familiar with whole blood viscosity.

I had read some arbitrary paper on whole blood viscosity. It was so compelling. The role of blood viscosity on a variety of diseases. I mean, my gosh, if you haven't seen the papers on whole blood viscosity, it's associated from everything from non-alcoholic fatty liver disease, gallstones, bone density osteoporosis, diabetes, the level of fatty liver in people with diabetes, cardiovascular disease, endothelial dysfunction, you name it. Then you read all these papers like, "Why are we not measuring viscosity?" I thought, "There's got to be someone out there who has figured out a way to calculate the viscosity by just using basic blood chemistry markers." It turns out that absolutely. But see, and again, I hadn't been taught this stuff. It was just me. I'll never forget it. I was up late one night. My kids had woken me up. I was just thinking about this. I started looking and –

JM: Of course. That's what most people think about when they wake up at 2 in the morning.

BW: Well, you don't understand. This has been a passion. There had to be – Because when you think about what contributes to viscosity – which by the way goes back to basic blood. What is in blood?

JM: Yeah.

BW: The most abundant thing in blood is protein. In terms of – it's mostly water. But then after water, it's protein in there, with albumin, globulin and fibrinogen. I was thinking, "Protein has to contribute to this, and protein's in the blood chemistry." Lo and behold, there's a validated calculation that looks at both low shear rate and high shear rate viscosity, that's been validated numerous times, that has been compared to actual whole blood viscosity. You know the two markers that it needs? Total protein and hematocrit. That's it.

JM: Wow.

BW: The studies on viscosity are so darn clear, and the conclusion on some of these papers that talk about this calculation is – I mean, it's the type of thing where if you read enough of these papers, you think, "Why are we not running this? Why are we not figuring this out?" The conclusion in some of these papers basically say, "Viscosity is such an issue." In fact, there's one paper. It's a hypothesis paper that hypothesizes that blood viscosity doesn't only contribute to Type 2 diabetes, but it's positive, which is in a profound and stable [inaudible 46:25].

It's such a thing. They say that it's so easy to calculate. It's been validated that every physician should be running this on every patient. But yet, where's that information? I came across this late one night and I had that thought. I said, "Why have we not been talking about this validated calculation on viscosity, which is an incredibly important parameter?" And then you go back into a clinical practice and you say that, "I can tell you more about what's going on in you than is actually on this lab, because calculations exist."

You probably heard about the fatty liver index. Fatty liver – if we have time – high-density lipoprotein (HDL) has been [inaudible 47:10] for a long time. There was a paper that looked at high levels of HDL and actually calling it dyslipidemia.

Usually, dyslipidemia means high cholesterol, high LDL, low HDL and abnormal triglycerides. But they were saying when HDL gets too high, even if it surpasses low-density lipoprotein (LDL), you should be calling that dyslipidemia too. That's not normal. In this paper, inclusion criteria was that you had to have fatty liver diagnosed by ultrasound. Everybody in this paper had fatty liver. They didn't report on this, although they had the table of the data. The average AST and ALT in all these people who had fatty liver was in the 20s. What are doctors usually using to diagnose fatty liver? The liver enzymes, right?

Thankfully, there's something called a fatty liver index that all you need is GGT, triglycerides, waist circumference and body mass index (BMI). It's fairly specific. It's pretty darn accurate as an indication of fatty liver. Here, all you need is a waist circumference. Somebody would calculate their BMI, look at their triglycerides and their GGT level. You can, with some confidence, predict whether they have fatty liver or not. Or at least, from a clinical decision-making perspective, decide if that's something that you want to pursue or not.

But where do you get that data? Off a basic blood chemistry, GGT and triglycerides. Osmolality is another calculation. You probably know this, but because of the way that water moves in the body, you have three major water compartments. You have, essentially, plasma. You have interstitial fluid and intercellular fluid. Researchers don't disagree on this. They disagree what to do about it.

They don't disagree on the fact that because of the way the water moves in osmotic gradients, that the osmolality of your blood is actually reflective of the osmolality intracellularly. You're not going to have an overly hydrated or dehydrated cell, and then your plasma's not going to reflect that. Why aren't we running viscosity and osmolality in calculating fatty liver in some people? When we have the data that's required and those are validated calculations, those are some other things that I cover in the weekend. The last one that I want to tell you is – Go ahead.

[-----50:00-----]

JM: Can you hold the last one? Because I just wanted to interject here. Because this is just beyond fascinating, which is why I'm so excited to attend your presentation in March, I believe, in Jacksonville, Florida. But people are not clinicians and are probably way in over their head right now. But a large number of the measurements that you're describing are actually calculated.

There is another alternative. Maybe you can talk about that now. But remember the thing you wanted to share, because we definitely want to get back to that. I just wanted to interject that I think you offer a service where you can actually provide the blood test for the persons themselves and take it through their blood-drawing site. They'll get it, then you run it through this program, this software program that's been developed, that actually takes or makes those calculations and make recommendations. Did I have that mixed up or is that right?

BW: No. It doesn't have all those calculations yet. We're still trying to work through some of those things. That will probably be another call, actually.

JM: Okay.

BW: No. I'm very, very excited about the prospects of that in the future as we work some bugs out for sure.

JM: Okay. Don't get discouraged if you're –

BW: No, no, no.

JM: It's common. You'll be able to take advantage of this incredible treasure trove of knowledge.

BW: Yes. Yeah.

JM: Get back to where you were before I interrupted you.

BW: The last one is this – Have you heard of the Intermountain health risk score?

JM: No.

BW: See? There again. There's the problem. Here's a guy like yourself who's more tapped into this industry than probably almost anybody else. But yet, you haven't heard about this. This was something that I stumbled across because I love blood chemistry. It's the best, most valuable, most accurate, most inexpensive test we could possibly be running. I get really frustrated as a functional medicine or naturopathic practitioner, that we're jumping on all these really expensive non-scientifically validated functional medicine tests when there's so much information that could be drawn from this.

I came across this. It's called an intermountain risk score. A lot has been done since I originally came across this, probably about five years ago. The short version is is in a hospital setting, tens of thousands of people have gone through this. They created a score based on basic blood

chemistry markers that should be on any lab test, mostly a complete blood count (CBC), differential type, and then a few chemistries, like sodium, potassium bicarbonate, mean platelet volume, which if you do Quest is always on there. But basic stuff.

What they did with tremendous accuracy was created a calculation. Let's say, hemoglobin. Your hemoglobin, at whatever marker or whatever value it was, you'd enter that one. If it was above and below with their range that they came up with, you might get two points. You enter your red blood cells. Then you enter hematocrit, mean corpuscular volume (MCV) glucose. They calculated. It has been talked about and published and republished so many times. It's a mortality risk score. But there's a 30-day, a one-year, and a five-year mortality risk essentially.

Hopefully, most people aren't so interested in the 30-day or one-year. But that five-year mortality risk score is so valuable when you think about this. Because you might have somebody who's, let's say, relatively healthy. That is self-prescribing a bunch of supplements, maybe exercising a little bit, trying to eat as healthy as they can. But physiologically, something's abnormal. They go to their doctor and everything looks pretty good. Let's say their glucose is good. If they were to enter in all these things, all these markers and it came out with a slightly high score, that's an indication that not everything is going well.

There was a paper, in fact, that was published based on all the work that this intermountain group has done. I forget the exact title, but it was something along the lines of, "In the genomic era, are we missing the low-hanging fruit?"

This author commended this group for doing this stuff, saying, "We are chasing the fancy, shiny objects in the newest, sexiest things in the best test in genomics, metabolomics, the biome and all this stuff. Yet, right smack in front of our face is the most inexpensive, scientifically validated test."

What this group has done is created a calculation where you can enter in those parameters. You can basically – Again, if the antithesis of optimal health is death, you can see where you are on this score. Maybe if your score doesn't come up great, then you can take it to someone who will actually take a look at what you're doing and make some recommendations to try and improve some of these things. That's just another example of there's more data inside of a blood chemistry test than the blood chemistry test is actually even reporting on. Things like osmolality. Things like viscosity. Things like the fatty liver index. Things like the Intermountain risk score.

JM: Do you have a link to that or a formula that can make the calculation?

BW: I don't think they publish their formula for obvious reasons. But if you type in intermountain risk score, one of the links that comes up is a calculator.

JM: Oh, perfect.

BW: You enter in the variables. You hit calculate and I think it tells you.

JM: Wow. Perfect.

BW: Unless you read some of their old studies. I think you could figure out the formula, which – I'm not saying anybody has or hasn't. There are good chances.

JM: While I was writing one of my previous books – actually, my last book is coming out in May, called KetoFast. I consulted with you and you gave me some insights on how to make the calculation of one of the researchers, so I appreciate that.

BW: Yeah. Well, you've got to dig in and you've got to read it all sometimes. But it's helpful. Otherwise, they patent it and try to hide it. That's fine. I respect that. Let's say I might do the same thing in those circumstances, but at the same time, the information is usually out there.

JM: This is really exciting. Let me just make some comments now, and I'll let you close. I'm thinking that if you're a clinician, you simply must attend this if you're treating patients. There's almost no excuse not to. It's in 30 cities in the United States. It's most likely within driving distance to where you're at. If it's not or if you're busy that weekend, well, you can go to another city you want to. You can fly there. Imagine that. But it's definitely something that's going to radically improve your ability to understand and make successful interclinical interventions to improve the health of your patients, relatively inexpensively.

I mean we're not talking fancy [inaudible 56:41] tests. This is general lab work that you're already doing on your patient. That would be my plea to you. Again, I'm going to be going to the Jacksonville event or presentation. If you want to meet up with me there, I'm glad to connect. But why don't you add your final words of wisdom or anything else that you think is important that we missed?

BW: No. I'm glad – I really do appreciate all your support on this. People don't go door-to-door anymore. We deliver everything online, emails and all these things. I'm a little too young, I think, to be old-fashioned, but I'm old-fashioned. [inaudible 57:17] for women, and teach your kids to say, "Thank you," and have respect for their elders. But another one is just, "Let's go to these cities, to people so that it makes it easier for them to attend." They don't have to worry of maybe flights or hotels as much. And teaching face-to-face and not just doing the online stuff, which I've done and that's fun and it's useful and it's valuable and it's accessible. You can really get in and the questions that are asked and the dialogue that takes place. I'm really excited about that.

In terms of the cost, I have to admit, without mentioning names, there are weekend seminars that are in the range of 1,500 dollars. It's so much money. I've seen these ones. The amount of clinical information you get is somewhat limited. Sometimes because there are multiple speakers. The cost of this, my goal – I'm trying to support my family – but my goal is to deliver so much information by lunch on the first day and that five hours of pre-event videos, without even considering the cost because [inaudible 58:20]. I really do hope to see people at this event. Go to DrWalsh.com. There's a small link for tour up in the top navigation bar. That will take you to the right page.

JM: Yeah. We'll definitely have a link on the page too.

[END]