## Introduction and Dr. McCormick's experience living with osteoporosis

Hey, Margie, here. What if osteoporosis Hey, Margie, here. What if osteoporosis and heart disease are more connected and heart disease are more connected than we realize? That's what today's than we realize? That's what today's episode is about. Osteoporosis expert episode is about. Osteoporosis expert Dr. Keith McCormick explains why bone Dr. Keith McCormick explains why bone loss and cardiovascular disease so often loss and cardiovascular disease so often show up together, the shared factors show up together, the shared factors that may be driving both, and what your that may be driving both, and what your blood work can reveal about your risk.

blood work can reveal about your risk. You'll learn which test to ask your You'll learn which test to ask your doctor for, what your routine blood work doctor for, what your routine blood work may already be telling you, and how may already be telling you, and how inflammation, metabolic health affect inflammation, metabolic health affect both your bones and your blood vessels.

both your bones and your blood vessels. Dr. Keith McCormick has been helping Dr. Keith McCormick has been helping people with osteoporosis since 1982.

people with osteoporosis since 1982. He's the author of Great Bones, Taking He's the author of Great Bones, Taking Control of Your Osteoporosis, which I Control of Your Osteoporosis, which I consider an encyclopedia on the subject consider an encyclopedia on the subject and recommend all the time. He's also and recommend all the time. He's also helped so many people in our community helped so many people in our community understand what may be contributing to understand what may be contributing to their bone loss, and what they can do to their bone loss, and what they can do to improve their bone health. So, this improve their bone health. So, this >> [music] >> [music] >> Welcome, Dr. McCormick. So happy to have >> Welcome, Dr. McCormick. So happy to have you here on the podcast. This is such an you here on the podcast. This is such an important topic, and when I asked you important topic, and when I asked you what do you think you would like to talk what do you think you would like to talk about, you said, "We need to discuss about, you said, "We need to discuss this because this is missing." So, thank this because this is missing." So, thank you so much for being here.

you so much for being here. >> Thanks for inviting me, Margie. Really >> Thanks for inviting me, Margie. Really appreciate it. appreciate it. >> Okay, so I know you have a lot of >> Okay, so I know you have a lot of information, and everybody listening, information, and everybody listening, don't worry if you don't get it all, but don't worry if you don't get it all, but this is just really important. So, I'm this is just really important. So, I'm going to turn it over to you, Dr.

going to turn it over to you, Dr. McCormick, and you can share your slides McCormick, and you can share your slides and get started. and get started. >> What I'm going to talk about today is >> What I'm going to talk about today is the shared roots of osteoporosis and the shared roots of osteoporosis and cardiovascular disease, and we're going cardiovascular disease, and we're going to talk about lab testing and how to go to talk about lab testing and how to go about that to help us not only identify about that to help us not only identify what's going on, but to understand what what's going on, but to understand what we're going to do for treatment, too.

we're going to do for treatment, too. So, let me tell you a little bit about So, let me tell you a little bit about my background. I guess it's important my background. I guess it's important because I have osteoporosis, which most because I have osteoporosis, which most people by now know if they know me at people by now know if they know me at all. And that's how I got into working all. And that's how I got into working with people with osteoporosis. I ended with people with osteoporosis. I ended up having a lot of fractures back when I up having a lot of fractures back when I was age 45. And I searched and searched was age 45. And I searched and searched for good doctor to work with. And after for good doctor to work with. And after five endocrinologists, I finally found five endocrinologists, I finally found this man in the right lower hand corner, this man in the right lower hand corner, Dr. Royce, from University of Dr. Royce, from University of Connecticut. And he was the actual Connecticut. And he

was the actual godfather of osteoporosis in the United godfather of osteoporosis in the United States. He was the number one guy. And States. He was the number one guy. And he took me under his wing. He not only he took me under his wing. He not only worked with me to help with my bone worked with me to help with my bone density, but also he taught me so much.

density, but also he taught me so much. And he was so open and such a kind man. And he was so open and such a kind man. And [clears throat] I owe a lot to him And [clears throat] I owe a lot to him because he taught me an awful lot about because he taught me an awful lot about osteoporosis. And one day he called me osteoporosis. And one day he called me up and he said, "Hey Keith, you know, I up and he said, "Hey Keith, you know, I can't go to NIH this weekend to meet can't go to NIH this weekend to meet with Camilla, the Duchess of Cornwall.

with Camilla, the Duchess of Cornwall. She's the president of the Royal She's the president of the Royal Osteoporosis Society. And And her Osteoporosis Society. And And her sidekick, Prince Charles, I can't go to sidekick, Prince Charles, I can't go to meet with them, but would you mind meet with them, but would you mind stepping in for me?" And so, I you know, stepping in for me?" And so, I you know, even though osteoporosis was very, very even though osteoporosis was very, very devastating to me, it's also done an devastating to me, it's also done an awful lot for me as far as awful lot for me as far as allowing me to meet with different allowing me to meet with different people. My world is so much bigger people. My world is so much bigger because of it. And then the biggest gift because of it. And then the biggest gift at all at all of all of all behind this is that I've gotten to work behind this is that I've gotten to work with so many patients and help them. I with so many patients and help them. I even got to meet with the Surgeon even got to meet with the Surgeon General back then when they wrote the General back then when they wrote the Surgeon General's report on bone health Surgeon General's report on bone health and and osteoporosis. And and and osteoporosis. And this was way back in the late, you know, this was way back in the late, you know, 1990s 1990s 1990s and early 2000s when people didn't and early 2000s when people didn't really know anything about osteoporosis.

really know anything about osteoporosis. There wasn't any major research. The The There wasn't any major research. The The drug companies weren't didn't have a lot drug companies weren't didn't have a lot of medications for it. So, I feel of medications for it. So, I feel honored and and fortunate that I was at honored and and fortunate that I was at the forefront of of much of this.

the forefront of of much of this. >> Yeah, Dr. McCormick, it's so >> Yeah, Dr. McCormick, it's so interesting, but I think even I really interesting, but I think even I really want this is to me the how long you've want this is to me the how long you've been involved and what's happened over been involved and what's happened over the years and how many people's lives the years and how many people's lives you've changed personally. But why don't you've changed personally. But why don't you tell people, I think just very you tell people, I think just very briefly, briefly, briefly, about your story so they know for those about your story so they know for those who don't know you why you are so who don't know you why you are so passionate. You didn't just sort of into passionate. You didn't just sort of into osteoporosis. So, why don't you just osteoporosis. So, why don't you just share real quickly where you you know, share real quickly where you you know, why you got into this and I think why you got into this and I think sometimes bad you know, sometimes when sometimes bad you know, sometimes when we struggle it turns into something we struggle it turns into something wonderful and I think that's what wonderful and I think that's what happens in your case.

happens in your case. >> It it certainly is. Yeah, I I didn't >> It it certainly is. Yeah, I I didn't really know anything about osteoporosis really know anything about osteoporosis back then. I'm a chiropractic physician.

back then. I'm a chiropractic physician. I knew a lot about, you know, I knew a lot about, you know, kinesiology and biomechanics and you kinesiology and biomechanics and you know, bone stuff, but not the metabolic know, bone stuff, but not the metabolic nature of bone. And so when I you know, nature of bone. And so when I you know, found out I had osteoporosis when I was found out I had osteoporosis when I was starting to break a lot I had broken a starting to break a lot I had broken a lot of bones throughout my life. And I lot of bones throughout my life. And I just knew I had to immerse myself in the just knew I had to immerse myself in the study of it to figure things out. And so study of it to figure things out. And so I've written two books on it, written a I've written two books on it, written a paper on it. I started a supplement paper on it. I started a supplement company Osteo Naturals. I now,

you know, company Osteo Naturals. I now, you know, have a my great bones education have a my great bones education information services where I do consults information services where I do consults with people with osteoporosis. So, it with people with osteoporosis. So, it has totally transformed my life. So, has totally transformed my life. So, yes, you're right. A bad thing certainly yes, you're right. A bad thing certainly turned into a good thing and and and I turned into a good thing and and and I said like I said, the biggest gift of said like I said, the biggest gift of all this is that I I feel like I can all this is that I I feel like I can help a lot of people not just because I help a lot of people not just because I know a lot about the the disorder, but I know a lot about the the disorder, but I think because I've been there and I have think because I've been there and I have a lot more awareness to what people are a lot more awareness to what people are going through when they when they find going through when they when they find out they have out they have fragile bones, you know.

fragile bones, you know. >> So, how many frac So, how many fractures >> So, how many frac So, how many fractures did you have prior to dealing with this?

did you have prior to dealing with this? >> Well, over my lifetime I've had 25. >> Well, over my lifetime I've had 25. >> Okay, and then you went from 25 >> Okay, and then you went from 25 fractures to doing Iron Man, right?

fractures to doing Iron Man, right? Which Which Which >> So, now I'm doing pretty good and I'll >> So, now I'm doing pretty good and I'll show you some slides later here at this show you some slides later here at this morning today about of a bone biopsy morning today about of a bone biopsy that I had. So, you'll kind of see the that I had. So, you'll kind of see the the shape that my bones were in at one the shape that my bones were in at one time. So, time. So, >> Okay, so let's continue but I just think >> Okay, so let's continue but I just think that's important cuz you're a role model that's important cuz you're a role model that this is possible. We can go from that this is possible. We can go from where you were to being strong, healthy, where you were to being strong, healthy, and really doing incredible exercise.

and really doing incredible exercise. Okay, so you let's let's move on. Okay, so you let's let's move on. >> So, today we're going to look at the >> So, today we're going to look at the connections between osteoporosis and connections between osteoporosis and cardiovascular disease.

cardiovascular disease. And the more scientists learn about And the more scientists learn about these two two diseases, the harder it these two two diseases, the harder it becomes to think of them as completely becomes to think of them as completely separate entities.

separate entities. They share multiple signaling pathways They share multiple signaling pathways and mechanisms that can simultaneously and mechanisms that can simultaneously drive bone loss on one hand and vascular drive bone loss on one hand and vascular injury and calcification on the other.

injury and calcification on the other. It's a phenomenon we call the calcium It's a phenomenon we call the calcium paradox. So, we're going to talk about paradox. So, we're going to talk about things like that and then we're going to things like that and then we're going to go look at a case. We'll call her Jane go look at a case. We'll call her Jane and she's a woman with both severe and she's a woman with both severe osteoporosis and cardiovascular disease.

osteoporosis and cardiovascular disease. And we're going to see how laboratory And we're going to see how laboratory biomarkers, lab tests, can tell us not biomarkers, lab tests, can tell us not just allow us to see what's happening just allow us to see what's happening physiologically, but why it's happening.

physiologically, but why it's happening. And most important, come up with a good And most important, come up with a good treatment program. Osteoporosis and treatment program. Osteoporosis and cardiovascular disease frequently travel cardiovascular disease frequently travel together. So, the next time you see your together. So, the next time you see your PCP or endocrinologist, I encourage you PCP or endocrinologist, I encourage you to ask them, "Hey, don't just look at my to ask them, "Hey, don't just look at my bone density. Look at my heart. Make bone density. Look at my heart. Make sure I'm okay on that that front, too." sure I'm okay on that that front, too.

## The connection between osteoporosis and cardiovascular health

" So, So, So, more than 10 million Americans have more than 10 million Americans have osteoporosis. And 50% of women, 16% of osteoporosis. And 50% of women, 16% of men will sustain a fracture because of men will sustain a fracture because of it. And half of all adults in the United it. And half of all adults in the United States have some level of cardiovascular States have some level of cardiovascular disease, and almost a million die each disease, and almost a million die each year. That's one person every 34 year. That's one person every 34 seconds. And we always talk about LDL, seconds. And we always talk about LDL, the low-density lipoproteins, as being a the low-density lipoproteins, as being a problem, but half of those people that problem, but half of those people that die have normal LDL cholesterol levels.

die have normal LDL cholesterol levels. So, if you have osteoporosis, your risk So, if you have osteoporosis, your risk for cardiovascular disease is four times for cardiovascular disease is four times higher than someone with normal bone higher than someone with normal bone density. And this isn't just because the density. And this isn't just because the calcium calcium calcium from the breakdown of your bones from the breakdown of your bones sprinkles over passively and gets lodged sprinkles over passively and gets lodged into your arteries. It's an active into your arteries. It's an active cell-mediated process, similar to what cell-mediated process, similar to what we see in the skeleton when your we see in the skeleton when your osteoblasts are forming bone. So, when osteoblasts are forming bone. So, when you osteoblasts form bone, there's a you osteoblasts form bone, there's a similar mechanism in your arteries that similar mechanism in your arteries that can make calcified plaque. So, we call can make calcified plaque. So, we call the shared biological mechanisms of the shared biological mechanisms of these two diseases the bone-vascular these two diseases the bone-vascular axis. This is the It's a unifying axis. This is the It's a unifying conceptual framework describing the conceptual framework describing the network of communication between bone network of communication between bone and the vascular system. It's a network and the vascular system. It's a network that shares many of the same risk that shares many of the same risk factors.

factors. factors. I list the lot of list risk factors I list the lot of list risk factors there, the aging, high lipids, sedentary there, the aging, high lipids, sedentary lifestyle, stress, all those things.

lifestyle, stress, all those things. Same risk factors for both disorders. Same risk factors for both disorders. So, chronic systemic inflammation is So, chronic systemic inflammation is probably the number one calling card of probably the number one calling card of these comorbidities. And we're going to these comorbidities. And we're going to talk about this signaling pathway called talk about this signaling pathway called the RANK-RANKL-OPG.

the RANK-RANKL-OPG. And I apologize for getting a little bit And I apologize for getting a little bit too complex here maybe for some people, too complex here maybe for some people, but I talk a lot about the but I talk a lot about the RANK-RANKL-OPG system in my book. And RANK-RANKL-OPG system in my book. And so, if you miss what I'm going to say so, if you miss what I'm going to say here, you can go there and look at that, here, you can go there and look at that, but it's really important to understand but it's really important to understand this system.

this system. So, RANKL, or it's called receptor So, RANKL, or it's called receptor activator for nuclear factor kappa-B activator for nuclear factor kappa-B ligand. So, the ligand is just a ligand. So, the ligand is just a molecule that signals are molecule that signals are The RANKL is a protein, a chemical The RANKL is a protein, a chemical signal that activates osteoclasts to signal that activates osteoclasts to break down bone. It's also a trigger to break down bone. It's also a trigger to for vascular calcification and and for vascular calcification and and destabilizing existing plaque in your destabilizing existing plaque in your arteries. So, this RANKL really ties arteries. So, this RANKL really ties these two diseases together.

these two diseases together. And you can't have elevated RANKL And you can't have elevated RANKL without having bone loss and damage to without having bone loss and damage to your blood vessels in the heart. This your blood vessels in the heart. This next one here is nitric oxide and that's next one here is nitric oxide and that's the [clears throat] smallest signaling the [clears throat] smallest signaling molecule and plays an integral part in molecule and plays an integral part in both diseases. And there's other other both diseases. And there's other other

shared things that that go along with shared things that that go along with the two diseases. Hormones, vitamin D, the two diseases. Hormones, vitamin D, vitamin K, sclerostin we're going to vitamin K, sclerostin we're going to talk about later, kidney disease, and of talk about later, kidney disease, and of course we have genetics. 50 to 70% of course we have genetics. 50 to 70% of our density is probably governed by our density is probably governed by genetics.

genetics. genetics. And thousands of genetic variants have And thousands of genetic variants have been discovered that influence bone been discovered that influence bone density. And for cardiovascular disease, density. And for cardiovascular disease, 40 to 60% of your risk 40 to 60% of your risk that was placed there by your parents' that was placed there by your parents' DNA. So, there's lots of genetic DNA. So, there's lots of genetic variants that have to do with the two variants that have to do with the two disorders. And these variants, they're disorders. And these variants, they're small changes in the DNA that can exert small changes in the DNA that can exert small incremental or what's called small incremental or what's called polygenic effects on bone and the polygenic effects on bone and the cardiovascular system. So, this is a cardiovascular system. So, this is a list of some of the most common variants list of some of the most common variants and I'm not going to talk about all of and I'm not going to talk about all of them but but they include inflammatory them but but they include inflammatory genes, estrogen, bone morphogenetic genes, estrogen, bone morphogenetic protein, nitric oxide production.

protein, nitric oxide production. But if you go to that middle one, the But if you go to that middle one, the APOE4, I'll just talk a little bit about APOE4, I'll just talk a little bit about that one specifically. And the reason that one specifically. And the reason why is because most of us think of the why is because most of us think of the APOE4 APOE4 APOE4 gene variant is just giving us increased gene variant is just giving us increased risk for Alzheimer's. But if you have risk for Alzheimer's. But if you have the APOE variant and even if you only the APOE variant and even if you only have one inherited copy, you can still have one inherited copy, you can still have increased fracture risk. And this have increased fracture risk. And this is due to its disruptive effect on is due to its disruptive effect on osteocyte function. Remember, we have osteocyte function. Remember, we have three three three bone cells. We have the osteoblast bone cells. We have the osteoblast that form bone, the osteoclast that tear that form bone, the osteoclast that tear down bone, and then the osteocytes that down bone, and then the osteocytes that they kind of govern the whole bone they kind of govern the whole bone remodeling system as a whole. And when remodeling system as a whole. And when you have this APOE you have this APOE genetic variant, it disrupts the genetic variant, it disrupts the function of osteocytes. So, they can't function of osteocytes. So, they can't really govern that bone remodeling really govern that bone remodeling system as well as they should. So, women system as well as they should. So, women with the APOE4 variant have a higher with the APOE4 variant have a higher fracture risk even if their bone mineral fracture risk even if their bone mineral density is not in the osteoporotic density is not in the osteoporotic range. And then we're going to talk range.

## MTHFR and homocysteine: why they matter

And then we're going to talk about these last three that MTHFR, about these last three that MTHFR, sclerostin, and then finally this really sclerostin, and then finally this really neat gene variant called SMG6. So, the neat gene variant called SMG6. So, the MTHFR gene, it codes for an enzyme that MTHFR gene, it codes for an enzyme that activates the activates the the vitamin folate.

the vitamin folate. And folate's a key cofactor for helping And folate's a key cofactor for helping us get rid of homocysteine. us get rid of homocysteine.

Homocysteine's a toxic metabolite Homocysteine's a toxic metabolite produced when you eat protein, produced when you eat protein, specifically the amino acid methionine.

specifically the amino acid methionine. And if a person has this MTHFR gene And if a person has this MTHFR gene variant, as many of us do, it's very variant, as many of us do, it's very common, then homocysteine levels common, then homocysteine levels increase in the blood.

increase in the blood. High homocysteine, especially when it High homocysteine, especially when it gets above 15 micromoles per liter, can gets above 15 micromoles per liter, can damage blood vessel walls, accelerate damage

blood vessel walls, accelerate plaque formation, promote clotting, and plaque formation, promote clotting, and bone it weakens the structural collagen bone it weakens the structural collagen crosslinks. It makes bones stiff, less crosslinks. It makes bones stiff, less flexible. And if it gets to 15 or 20 flexible. And if it gets to 15 or 20 micromoles per liter, it can increase micromoles per liter, it can increase fracture risk two to three times.

fracture risk two to three times. >> Hey Wajeeha. As a physical therapist, I >> Hey Wajeeha. As a physical therapist, I know firsthand how important exercise is know firsthand how important exercise is for our bones, overall health, and for our bones, overall health, and happiness. [music] happiness. [music] And unfortunately, there's a lot of And unfortunately, there's a lot of confusion on what exercises are safe and confusion on what exercises are safe and effective for people with osteoporosis.

effective for people with osteoporosis. [music] [music] [music] That's why I created this handout that That's why I created this handout that contains a 30-minute video [music] where contains a 30-minute video [music] where I explain the concepts so you understand I explain the concepts so you understand the do's and don'ts [music] when it the do's and don'ts [music] when it comes to exercise. And this is important comes to exercise. And this is important because this way you can go into any because this way you can go into any class and know what you should be doing class and know what you should be doing and what [music] you should avoid and what [music] you should avoid because too many people are doing because too many people are doing exercises that [music] actually increase exercises that [music] actually increase their risk of spinal fractures.

their risk of spinal fractures. I also included videos of me I also included videos of me demonstrating [music] demonstrating [music] effective balance, posture, and effective balance, posture, and weight-bearing exercises [music] you can weight-bearing exercises [music] you can put into your day right away. So, all put into your day right away. So, all you need to do to access this [music] you need to do to access this [music] handout, it's free, is go to handout, it's free, is go to tinyurl.com/osteoporosisexercises.

So, it's t i n y u r l.com So, it's t i n y u r l.com >> [music] >> [music] >> [music] >> /osteoporosisexercises or you can click the link in the show or you can click the link in the show [music] notes. Now, back to the show.

[music] notes. Now, back to the show. Yeah, we have to stop here for a second Yeah, we have to stop here for a second because this is so important. It's not because this is so important. It's not an expensive test, but yet Dr. McCombs, an expensive test, but yet Dr. McCombs, most doctors are not ordering this as most doctors are not ordering this as part of their routine. And a lot of part of their routine. And a lot of people What number The thing is, if it's people What number The thing is, if it's 14, it will show up as normal on a lot 14, it will show up as normal on a lot of of of >> Yeah.

>> Yeah. >> Yeah. >> So, what what are the value What value >> So, what what are the value What value do you like to see it below when you do you like to see it below when you >> I like to keep it at eight or below or >> I like to keep it at eight or below or so. But, if it's a if it's a nine, it's so. But, if it's a if it's a nine, it's not a big deal. But, yes, when you start not a big deal. But, yes, when you start getting to 12, 13, 14, that's of of getting to 12, 13, 14, that's of of concern.

concern. concern. >> What I like about this is though, even >> What I like about this is though, even if you don't test, you don't have to if you don't test, you don't have to find You don't have to do the MTHFR the find You don't have to do the MTHFR the MTHFR test, but if you see your MTHFR test, but if you see your homocysteine is elevated, there's a homocysteine is elevated, there's a really simple treatment. You want to really simple treatment. You want to just talk about what you do when you just talk about what you do when you find someone has this elevated Yeah.

find someone has this elevated Yeah. >> Yeah, to get the MTHFR test, I don't >> Yeah, to get the MTHFR test, I don't know, it's a 100 bucks or 150 bucks or know, it's a 100 bucks or 150 bucks or something like that. I I I don't ever something like that. I I I don't ever test for it, so that's why I don't test for it, so that's why I don't really know the number. But, a really know the number. But, a homocysteine test is is maybe like $20.

homocysteine test is is maybe like $20. So, it's it's much less expensive to So, it's it's much less expensive to get.

Yes, as you said, everybody should get. Yes, as you said, everybody should get it. And I always There's a lot of get it. And I always There's a lot of companies that sell products that help companies that sell products that help cofactors for the enzyme that breaks the cofactors for the enzyme that breaks the homocysteine down back in either to homocysteine down back in either to methionine or gets rid of it. But, the methionine or gets rid of it. But, the cofactors like vitamin B2, B6, B12, cofactors like vitamin B2, B6, B12, trimethylglycine. I I use a Designs for trimethylglycine. I I use a Designs for Health product called Homocysteine Health product called Homocysteine Supreme. Almost always, it'll take a Supreme. Almost always, it'll take a homocysteine from a 15 and bring it homocysteine from a 15 and bring it right down to 10 or 8 or something like right down to 10 or 8 or something like that. So, that. So, yes, it's a cheap test to get, yes, it's a cheap test to get, inexpensive test to get, and it's easy inexpensive test to get, and it's easy to to fix.

to to fix. >> And has significant implications for >> And has significant implications for both our bones and our cardiovascular both our bones and our cardiovascular and inflammation. So, I think it's and inflammation. So, I think it's something that everybody needs to something that everybody needs to >> Everybody should test for.

>> Everybody should test for. >> Put on their radar. >> Put on their radar. >> So, this is a a Everybody's probably >> So, this is a a Everybody's probably familiar with with sclerostin. If you familiar with with sclerostin. If you especially if you if you're familiar especially if you if you're familiar with the osteoporosis medication with the osteoporosis medication romosozumab, romosozumab, romosozumab, or what's called Evenity, then you've or what's called Evenity, then you've probably heard of sclerostin. It's a probably heard of sclerostin. It's a protein that your body produces to keep protein that your body produces to keep osteoblasts from producing too much osteoblasts from producing too much bone. And I mean, you know, we always bone. And I mean, you know, we always talk about osteoporosis as too little talk about osteoporosis as too little bone, but we also don't want to have too bone, but we also don't want to have too much bone, and that's where sclerostin much bone, and that's where sclerostin comes in. It's also an important comes in. It's also an important molecular link between bone and the molecular link between bone and the vascular systems. Evenity is an antibody vascular systems. Evenity is an antibody against sclerostin, so it it keeps it against sclerostin, so it it keeps it down since And since sclerostin prevents down since And since sclerostin prevents your osteoblasts from forming too much your osteoblasts from forming too much bone, taking it away taking that bone, taking it away taking that sclerostin away leads to increased bone sclerostin away leads to increased bone density.

density. density. And that's exactly what happens when we And that's exactly what happens when we have a sclerostin gene variant. So, have a sclerostin gene variant. So, there's three basic types of variants there's three basic types of variants for for this sclerostin gene, but only for for this sclerostin gene, but only only going to be talking about one of only going to be talking about one of them. It's the mildest form of all. It's them. It's the mildest form of all. It's relatively common. That's why I wanted relatively common. That's why I wanted to mention it. And it's a loss of to mention it. And it's a loss of function variant. So, in other words, it function variant. So, in other words, it causes a slightly reduced sclerostin causes a slightly reduced sclerostin activity. If a person has this mild activity. If a person has this mild variant, it can result in like a 0.2, variant, it can result in like a 0.2, maybe 0.3 standard deviation higher bone maybe 0.3 standard deviation higher bone density compared to somebody without the density compared to somebody without the variant. So, it's not a a huge impact on variant. So, it's not a a huge impact on density, but it's it's it's worth density, but it's it's it's worth noting. So, let's say you have a bone noting. So, let's say you have a bone density density density of a spine T-score of -2.7.

of a spine T-score of -2.7. And you have that's a fracture risk for And you have that's a fracture risk for sure, but it's not awful. But, you also sure, but it's not awful. But, you also happen to carry a mild loss of function happen to carry a mild loss of function sclerostin variant variant, which you sclerostin variant variant, which you don't know about cuz you haven't done don't know about cuz you haven't done genetic testing, which I'm not genetic testing, which I'm not suggesting you should, but which makes suggesting you should, but which makes your bone density not quite as low as it your bone density not quite as low as it otherwise would be. In other words, the otherwise would be. In other words, the variant could partially mask the variant could partially mask the severity of your bone loss. Now, add a severity of your bone loss. Now, add a few other complications to this few other complications to this scenario.

scenario. scenario. Your DEXA scan was performed Your DEXA scan was performed incorrectly, not uncommon,

and incorrectly, not uncommon, and exaggerated the degree of your bone exaggerated the degree of your bone loss.

loss. loss. You're also small, you're petite, you're You're also small, you're petite, you're less than 5 ft, you're only 98 lb. So, less than 5 ft, you're only 98 lb. So, your bone density looks worse on paper your bone density looks worse on paper than it really is because remember bone than it really is because remember bone density scan is a two-dimensional density scan is a two-dimensional picture of a three-dimensional object.

picture of a three-dimensional object. So, so smaller people look a little bit So, so smaller people look a little bit worse on paper than they really are.

worse on paper than they really are. Plus, your lipid panel is off. You have Plus, your lipid panel is off. You have high LDL lipids, you have a high APOB, high LDL lipids, you have a high APOB, you have high LP little a, a genetic you have high LP little a, a genetic indicator that you have your LDLs are indicator that you have your LDLs are more sticky to they have a more chance more sticky to they have a more chance of sticking to the side of the wall and of sticking to the side of the wall and causing plaque formation in your causing plaque formation in your vessels. So, these things are elevated, vessels. So, these things are elevated, so it does put you so it does put you >> [clears throat] >> [clears throat] >> [clears throat] >> this person at a higher risk for >> this person at a higher risk for cardiovascular disease. But, this cardiovascular disease. But, this person's person's person's doctor doctor doctor just got concerned about her T score, just got concerned about her T score, about her apparent fracture risk, just about her apparent fracture risk, just by looking at her T score, and by looking at her T score, and prescribed Evenity.

prescribed Evenity. But, in reality, you didn't really need But, in reality, you didn't really need it because you not only had a sclerostin it because you not only had a sclerostin variant, but your DEXA was wrong. And variant, but your DEXA was wrong. And you're petite. So, in this scenario, you're petite. So, in this scenario, there's a possibility that there's a possibility that cardiovascular risk associated with cardiovascular risk associated with Evenity could be a tad bit higher in Evenity could be a tad bit higher in this setting.

this setting. Proposed mechanism behind this Proposed mechanism behind this cautionary tale is this. Genetic cautionary tale is this. Genetic variants like this affect bone and can variants like this affect bone and can increase vascular inflammation and increase vascular inflammation and encourage arterial calcification. So, in encourage arterial calcification. So, in other words, you become, at least other words, you become, at least theoretically, at more cardiovascular theoretically, at more cardiovascular risk. And this risk is even greater if risk. And this risk is even greater if you have chronic kidney disease. So, the you have chronic kidney disease. So, the question is this. Is this a good idea to question is this. Is this a good idea to prescribe this woman Evenity? Well, the prescribe this woman Evenity? Well, the research on these effects are research on these effects are conflicting. And thankfully, any conflicting. And thankfully, any additional cardiovascular risk additional cardiovascular risk associated with this variant, with or associated with this variant, with or without Evenity, is likely to be small without Evenity, is likely to be small if it exists at all.

if it exists at all. But, But, But, it's still something worth understanding it's still something worth understanding because we do not have all the answers because we do not have all the answers yet. And that's why prescribing yet. And that's why prescribing physicians need to consider the physicians need to consider the patient's broader vascular patient's broader vascular cardiovascular risk. And that's by cardiovascular risk. And that's by getting a more comprehensive lipid getting a more comprehensive lipid profile, not just triglycerides, you profile, not just triglycerides, you know, cholesterol, HDL. They need to know, cholesterol, HDL. They need to look at APOB, at LP, need to look at the look at APOB, at LP, need to look at the number and size of the LDL particles.

number and size of the LDL particles. And they often need to look at a And they often need to look at a person's metabolic health, what their person's metabolic health, what their glucose levels are is are, and their glucose levels are is are, and their fasting insulin. And the reason why is fasting insulin. And the reason why is because it's it's a lot of times it's because it's it's a lot of times it's it's a background of inflammation and it's a background of inflammation and possibly possibly possibly glucose handling, metabolic handling glucose handling, metabolic handling issues that actually cause injury to issues that actually cause injury to that wall, allowing the LDL particles

to that wall, allowing the LDL particles to get in there and cause plaque.

get in there and cause plaque. So, So, So, we have to look at the metabolic health we have to look at the metabolic health of the person also. of the person also.

>> Okay. Before we go on, this is such an >> Okay. Before we go on, this is such an important topic, actually, because we important topic, actually, because we both know A vanities an incredible drug both know A vanities an incredible drug when it's used in the right person, and when it's used in the right person, and it's helped so many people. But, what it's helped so many people. But, what I've been seeing in people in my I've been seeing in people in my community, and Dr. Millman and uh community, and Dr. Millman and uh practitioners, people are seeing, Dr.

practitioners, people are seeing, Dr. McCormack, that they're not getting McCormack, that they're not getting these complete, you know, they may they these complete, you know, they may they may send them, someone wants to put the may send them, someone wants to put the endocrinologist wants to put the person endocrinologist wants to put the person on A vanity, so they send them to the on A vanity, so they send them to the cardiologist, but they're just doing cardiologist, but they're just doing very routine things. And so, they could very routine things. And so, they could be missing this. So, what you're saying, be missing this. So, what you're saying, I just want to clarify, is they don't I just want to clarify, is they don't need to do the genetic testing, but they need to do the genetic testing, but they need to do this complete cardiovascular need to do this complete cardiovascular workup. And what do you find is workup. And what do you find is typically missing? What test, typically missing? What test, specifically?

specifically? specifically? >> Well, they the end >> Well, they the end >> Or the >> Or the >> APOB, the LP little A, and what what's >> APOB, the LP little A, and what what's called an NMR, a nuclear magnetic called an NMR, a nuclear magnetic resonance, where they can look at the resonance, where they can look at the the size and the and the number of those the size and the and the number of those LDL particles, cuz if you have really LDL particles, cuz if you have really small LDL particles, they have easier small LDL particles, they have easier time to get in through that vessel wall time to get in through that vessel wall and and cause plaque. So, yes, it's a and and cause plaque. So, yes, it's a more of a comprehensive lipid panel, but more of a comprehensive lipid panel, but it's not terribly, terribly expensive it's not terribly, terribly expensive either, and and should be done. And and either, and and should be done. And and the the message I'm trying to get across the the message I'm trying to get across here is context is everything. You need here is context is everything. You need to look at it more than just taking a to look at it more than just taking a quick glance at the DEXA T score and quick glance at the DEXA T score and prescribing medication. And no, I'm not prescribing medication. And no, I'm not suggesting that everybody should suggesting that everybody should get sclerostin gene testing. I'm not get sclerostin gene testing. I'm not saying that at all. But, for most cases saying that at all. But, for most cases of osteoporosis and cardiovascular of osteoporosis and cardiovascular disease, genetic testing is not that disease, genetic testing is not that helpful at at at least at this stage of helpful at at at least at this stage of of technology and our clinical of technology and our clinical understanding, genetic testing it can understanding, genetic testing it can indicate possible risk polygenic nature indicate possible risk polygenic nature of the two diseases, but it the reports of the two diseases, but it the reports usually don't really help us much at at usually don't really help us much at at all really in the clinic. It's different all really in the clinic. It's different if we're trying to confirm, you know, if we're trying to confirm, you know, specific genetic conditions such as specific genetic conditions such as osteogenesis imperfecta and things like osteogenesis imperfecta and things like that, but for for the typical that, but for for the typical osteoporosis patient, osteoporosis patient, no, I don't I don't recommend going to no, I don't I don't recommend going to that expense.

that expense. >> Yeah, so I just wanted to say one more >> Yeah, so I just wanted to say one more thing because this is a very popular thing because this is a very popular medication and it is helping a lot of medication and it is helping a lot of people and there is significant, you people and there is significant, you know, improvements that we see with this know, improvements that we see with this and so my question to you is what will and so my question to you is what will happen? Like what would happen if this happen? Like what would happen if this if this person or someone with these if this person or someone with these cardiovascular issues goes on, you know, cardiovascular issues goes on, you know, what goes on and what are the possible what goes on and what are the possible side effects?

side effects? >> I do think the cardiovascular risk can >> I do think the cardiovascular risk can increase and I

mean, that's my opinion, increase and I mean, that's my opinion, you know, we'll we'll know later on in you know, we'll we'll know later on in 10 probably 10 years from now, 10 probably 10 years from now, but you know, and and as you said, I'm but you know, and and as you said, I'm not against Evenity. I I've had many not against Evenity. I I've had many patients on Evenity that's helped patients on Evenity that's helped tremendously, but I've also had doctors tremendously, but I've also had doctors prescribe it when a person has a prescribe it when a person has a negative 2.6 or 2.7 and and they're not negative 2.6 or 2.7 and and they're not fracturing and then that doesn't make fracturing and then that doesn't make any sense to me. So, we need to do any sense to me. So, we need to do our homework and make sure we know the our homework and make sure we know the risk of that patient before we make risk of that patient before we make decisions.

decisions. decisions. >> Yeah, and we have seen in the community >> Yeah, and we have seen in the community people that haven't gone to that and people that haven't gone to that and have had some issues. So, I think this have had some issues. So, I think this is just such an important point. So, is just such an important point. So, thank you so much for bringing this up.

thank you so much for bringing this up. >> So, the other thing that you know, as I >> So, the other thing that you know, as I said, you know, said, you know, regular genetic testing doesn't help us regular genetic testing doesn't help us that much for these little variants, but that much for these little variants, but now we're trying now we're trying to now we're trying now we're trying to see which see which gene disorders, which gene variants can gene disorders, which gene variants can cause pleiotropic effect. In other cause pleiotropic effect. In other words, one gene might affect words, one gene might affect two or three different disorders.

two or three different disorders. And this next slide talks about this And this next slide talks about this gene variant called SMG6. gene variant called SMG6.

And I'm incredibly excited about it And I'm incredibly excited about it because so last year at Harvard, they because so last year at Harvard, they identified 211 identified 211 shared genes between bone density and shared genes between bone density and coronary artery calcifications. And coronary artery calcifications. And researchers revealed specific localized researchers revealed specific localized pathways, especially oxidative stress pathways, especially oxidative stress pathways and protein degradation pathways and protein degradation pathways, that directly connected these pathways, that directly connected these two diseases. And that chromosome 17 was two diseases. And that chromosome 17 was a major chromosome involved. It has a major chromosome involved. It has about 1,200 protein coding genes and one about 1,200 protein coding genes and one of them is SMG6. So, what's SMG6 do? And of them is SMG6. So, what's SMG6 do? And the reason why I'm so excited about it the reason why I'm so excited about it is because it does have application, I is because it does have application, I think, to not most of us, but some of us think, to not most of us, but some of us might have both the comorbidity that of might have both the comorbidity that of osteoporosis and cardiovascular disease.

osteoporosis and cardiovascular disease. So, SMG6 makes an enzyme that cuts away So, SMG6 makes an enzyme that cuts away faulty readings of mRNA. So, it's like a faulty readings of mRNA. So, it's like a molecular scissors that cuts out protein molecular scissors that cuts out protein defects and and it also has a disposal defects and and it also has a disposal system or a shredder-like system that system or a shredder-like system that destroys worn-out proteins or proteins destroys worn-out proteins or proteins that have been misfolded or or damaged.

that have been misfolded or or damaged. And if SMG6 is impaired, damaged And if SMG6 is impaired, damaged proteins pile up and we have increased proteins pile up and we have increased oxidative stress and tissue oxidative stress and tissue dysregulation. It causes us to a feeling dysregulation. It causes us to a feeling have feelings of really drained energy have feelings of really drained energy and and increase of the aging process.

and and increase of the aging process. So, the reason why I bring this up is So, the reason why I bring this up is because genes can be dramatically because genes can be dramatically involved in regulating our bone involved in regulating our bone strength. And you know, completely strength. And you know, completely diagnosing, completely figuring out diagnosing, completely figuring out what's going on, why a person has bone what's going on, why a person has bone loss can be impossible because genetics loss can be impossible because genetics like possibly a SMG6 variant, we can't like possibly a SMG6 variant, we can't you know, we don't know that. And even

you know, we don't know that. And even if you had the SMG6 tested, we still if you had the SMG6 tested, we still don't know if that's really causing any don't know if that's really causing any of your issues. So, at this point you of your issues. So, at this point you know, testing I'm not advocating, but know, testing I'm not advocating, but there are things like this that are there are things like this that are important. And when I look at this SMG6 important. And when I look at this SMG6 and then I look at a patient that you and then I look at a patient that you know, some of my patients that have know, some of my patients that have extremely low P1NP, which is the lab extremely low P1NP, which is the lab marker for osteoblastic activity, and marker for osteoblastic activity, and they have a crazy high C-terminal they have a crazy high C-terminal propeptide P1NP ratio. So, their CTX is propeptide P1NP ratio. So, their CTX is high and their P1NP is doesn't match high and their P1NP is doesn't match that CTX. And we can talk about that that CTX. And we can talk about that ratio business later, but when I see ratio business later, but when I see that kind of thing, when I see studies that kind of thing, when I see studies like this for the SMG6 as well, maybe like this for the SMG6 as well, maybe we're we're starting to get closer to we're we're starting to get closer to finding the answers to why somebody finding the answers to why somebody might have really, really low P1NP.

might have really, really low P1NP. Because their ability for their blast to Because their ability for their blast to function is less because of a gene a function is less because of a gene a gene variant. Okay, we'll go on. So, gene variant. Okay, we'll go on. So, where do we start? How do we look at a where do we start? How do we look at a patient? What do we do? How do we figure patient? What do we do? How do we figure out what's going on? The answer is out what's going on? The answer is everywhere. We just have to look under everywhere.

## The deeper lab testing approach

We just have to look under the rocks. And laboratory testing is the rocks. And laboratory testing is what helps us look under those rocks. what helps us look under those rocks.

And so, for osteoporosis, we don't just And so, for osteoporosis, we don't just look for vitamin low vitamin D or just look for vitamin low vitamin D or just you know, elevated calcium or you know, elevated calcium or parathyroid hormone that indicates parathyroid hormone that indicates hyperparathyroidism hyperparathyroidism hyperparathyroidism or low TSH for an overactive thyroid.

or low TSH for an overactive thyroid. Yes, those are important, but they are Yes, those are important, but they are very easy to spot. And that's usually very easy to spot. And that's usually not finding out the cause of somebody's not finding out the cause of somebody's bone loss is is usually not that easy.

bone loss is is usually not that easy. We have to look at We have to look at all the labs. We look for abnormal all the labs. We look for abnormal patterns, trends, red flags, and hidden patterns, trends, red flags, and hidden clinical correlations. So, we're going clinical correlations. So, we're going to go through some of those right now.

to go through some of those right now. For cardiovascular disease, as we talked For cardiovascular disease, as we talked about earlier just now, you have to get about earlier just now, you have to get more than just a basic lipid panel.

more than just a basic lipid panel.

## Janeu2019s case: severe osteoporosis and cardiovascular disease

So, for example, LP little A, APOB, this So, for example, LP little A, APOB, this NMR testing for the LDL size and NMR testing for the LDL size and particle number, and so I mentioned particle number, and so I mentioned metabolic health, the hemoglobin A1C, metabolic health, the hemoglobin A1C, fasting insulin, those things are fasting insulin, those things are important to get. So, let's go to Jane important to get. So, let's go to Jane and we'll and we'll see how lab testing and we'll and we'll see how lab testing helped us here. So, Jane is 52, helped us here. So, Jane is 52, post menopause. Uh she was a marathon post menopause. Uh she was a marathon runner. She had a heavy use of NSAIDs runner. She had a heavy use of NSAIDs because of that, which I knew right away because of that, which I knew right away to look for a gut issues possibly with to look for a gut issues possibly with

her. Uh she was on rosuvastatin 10 mg her. Uh she was on rosuvastatin 10 mg because she had cardiovascular disease.

because she had cardiovascular disease. So, her mom had osteoporosis, her dad So, her mom had osteoporosis, her dad died of heart failure or a heart attack.

died of heart failure or a heart attack. Jane herself had several fractures, a T8 Jane herself had several fractures, a T8 compression fracture, forearm, multiple compression fracture, forearm, multiple lower extremity uh stress fractures. Her lower extremity uh stress fractures. Her T-score was a -4.3 in her spine, and she T-score was a -4.3 in her spine, and she had several 50% blockages in the had several 50% blockages in the arteries around her heart. So, she arteries around her heart. So, she definitely had a cardiovascular issue, definitely had a cardiovascular issue, and it was a good thing she was on the and it was a good thing she was on the rosuvastatin.

rosuvastatin. rosuvastatin. So, when Jane went to see her So, when Jane went to see her cardiologist at the beginning of this cardiologist at the beginning of this whole thing, she asked, "What can I do, whole thing, she asked, "What can I do, you know, to help my cardiovascular you know, to help my cardiovascular issue, you know, all this plaque in my issue, you know, all this plaque in my in my arteries and stuff?" And and her in my arteries and stuff?" And and her doctor just said, "Take your doctor just said, "Take your rosuvastatin. That's all you can do." rosuvastatin. That's all you can do." The doctor didn't even know that she had The doctor didn't even know that she had osteoporosis. It might have been in her osteoporosis. It might have been in her chart, but did she care about it? I chart, but did she care about it? I don't know. And I think that's the don't know. And I think that's the failing of the system. You we are in a failing of the system. You we are in a population-based industrialized medicine population-based industrialized medicine system, and doctors system, and doctors are in a bad situation. They're pushed are in a bad situation. They're pushed beyond their ability to give good care beyond their ability to give good care sometimes by the whole industry. And so, sometimes by the whole industry. And so, we as patients have a difficult time, I we as patients have a difficult time, I think, getting good health care think, getting good health care sometimes. So, I don't fault doctors, I sometimes. So, I don't fault doctors, I fault the system. And I think your fault the system. And I think your doctor, in general, is incredibly doctor, in general, is incredibly interested in helping you out, but they interested in helping you out, but they have time constraints. So, you have to have time constraints. So, you have to fight for your own health here and try fight for your own health here and try to encourage your doctor to look and see to encourage your doctor to look and see if you do have osteoporosis, just have if you do have osteoporosis, just have them check take a look at your them check take a look at your cardiovascular health, too. Okay. So, cardiovascular health, too. Okay. So, when Jane came to me, when Jane came to me, these are the lab tests that I got. I I these are the lab tests that I got. I I separate them here. There There's separate them here. There There's overlap, of course, but overlap, of course, but I The typical osteoporosis labs are on I The typical osteoporosis labs are on the left. The typical ones are the left. The typical ones are cardiovascular system are on the right.

cardiovascular system are on the right. Like I said, there's overlap, but And I Like I said, there's overlap, but And I And you don't have to get all these And you don't have to get all these tests, and that's not what I'm saying. I tests, and that's not what I'm saying. I bolded the ones that I think are the bolded the ones that I think are the most important. So, we're going to go most important. So, we're going to go through this for a couple minutes here through this for a couple minutes here and see how to work with some of these and see how to work with some of these labs. For labs. For the your bone health and how it's either the your bone health and how it's either building up or tearing down, the building up or tearing down, the C-telopeptide and the P1NP are probably C-telopeptide and the P1NP are probably the most important to get. So, CTX or the most important to get. So, CTX or C-telopeptide C-telopeptide C-telopeptide is the bone resorption marker. It is the bone resorption marker. It measures osteoclastic activity. And for measures osteoclastic activity. And for every every every increased standard deviation increase of increased standard deviation increase of CTX, your fracture risk will increase CTX, your fracture risk will increase 27%.

27%. 27%. So, So, So, we say, "What's a standard deviation?" we say, "What's a standard deviation?" Well, Well, Well, that's hard to really explain and and that's hard to really explain and and but for an example, if you had a 400 CTX but for an example, if you had a 400 CTX versus a 600 CTX, that would be about versus a 600 CTX, that would be about one standard deviation. So, going from a one standard deviation. So, going from a 400 to 600

really does increase fracture 400 to 600 really does increase fracture risk. And we want to keep CTX risk. And we want to keep CTX 400 or below, about. P1NP, that's the 400 or below, about. P1NP, that's the bone formation or osteoblastic activity.

bone formation or osteoblastic activity. And it's nice to try to keep these two And it's nice to try to keep these two within a ratio of 10:1, 9:1, some ratio, within a ratio of 10:1, 9:1, some ratio, something like that. Jane had a ratio of something like that. Jane had a ratio of 14:1. So, so either way too much clastic 14:1. So, so either way too much clastic activity or not nearly enough blastic activity or not nearly enough blastic activity, but her ratio was very poor.

activity, but her ratio was very poor. Celiac testing. So, we want to make sure Celiac testing. So, we want to make sure that a person doesn't have celiac that a person doesn't have celiac disease or even to have a sensitivity to disease or even to have a sensitivity to gluten because that can increase gluten because that can increase antibodies which increase osteoclastic antibodies which increase osteoclastic activity. I always tell patients one of activity. I always tell patients one of the most important things I tell them is the most important things I tell them is your osteoclast is a form of a white your osteoclast is a form of a white blood cell. In other words, anything blood cell. In other words, anything that ramps up your immune system and that ramps up your immune system and spews out more either if you have more spews out more either if you have more oxidative stress, free radicals, you oxidative stress, free radicals, you have more pro-inflammatory cytokines, have more pro-inflammatory cytokines, anything that riles up that immune anything that riles up that immune system will probably talk to the system will probably talk to the osteoclast and then they have one action osteoclast and then they have one action and that is to tear down bone. So, and that is to tear down bone. So, things like having a celiac test to make things like having a celiac test to make sure you're not not just that there's sure you're not not just that there's not damage to the endocytes in them in not damage to the endocytes in them in the vessel in the intestinal wall, but the vessel in the intestinal wall, but that you're not even having a antibody that you're not even having a antibody reaction to gluten. That's important.

reaction to gluten. That's important. Just the same as it's important to look Just the same as it's important to look at the gut. Well, I have a slide later at the gut. Well, I have a slide later on about where we'll look at the gut and on about where we'll look at the gut and how important that is because 70% of how important that is because 70% of your immune system is in your digestive your immune system is in your digestive tract, is in your gut. So, when you tract, is in your gut. So, when you have digestive issues, gut issues, bacterial digestive issues, gut issues, bacterial overgrowth, you often will affect those overgrowth, you often will affect those osteoclasts. Vitamin D, PTH, CBC, CMP, osteoclasts. Vitamin D, PTH, CBC, CMP, the comprehensive metabolic profile, the comprehensive metabolic profile, these are all really important tests to these are all really important tests to get. And on the cardiovascular side, as get. And on the cardiovascular side, as I mentioned earlier, we need to do I mentioned earlier, we need to do a much better job at getting a more a much better job at getting a more comprehensive profile on people. APOB, comprehensive profile on people. APOB, LP little A, the high sensitivity LP little A, the high sensitivity C-reactive protein. That's a It's a C-reactive protein. That's a It's a generalized inflammatory marker. It's generalized inflammatory marker. It's not specific, but it can help look out not specific, but it can help look out for for chronic systemic inflammation.

for for chronic systemic inflammation. Homocysteine, we already talked about Homocysteine, we already talked about that. And these numbers after that, I that. And these numbers after that, I didn't mention those are Jean Jane's didn't mention those are Jean Jane's values. So, like what APOB, you know, values. So, like what APOB, you know, you really need to keep that below 80.

you really need to keep that below 80. She was in 83. Homocysteine was way up She was in 83. Homocysteine was way up at 14.8. Hemoglobin A1C was right at at 14.8. Hemoglobin A1C was right at borderline of pre-diabetes. So, you borderline of pre-diabetes. So, you know, she did have a a terrible diet, know, she did have a a terrible diet, and so we had to work with that. Then and so we had to work with that. Then there's some other ones here, the LDH.

there's some other ones here, the LDH. We're going to talk about the TMAO and We're going to talk about the TMAO and ADMA. ADMA. ADMA. But, you know, you everybody doesn't But, you know, you everybody doesn't have to get those. That's not what I'm have to get those. That's not what I'm saying. I'm saying that there is a whole

saying. I'm saying that there is a whole battery of tests for osteoporosis, for battery of tests for osteoporosis, for cardiovascular disease, that can really cardiovascular disease, that can really paint paint paint the picture, a very nice picture of the picture, a very nice picture of what's going on in a patient's what's going on in a patient's physiology. Okay, so let's go to the physiology.

## The RANK/RANKL/OPG pathway connecting bones and blood vessels

Okay, so let's go to the next slide. So, as I promised earlier, next slide. So, as I promised earlier, I'm going to talk about this rank rankle I'm going to talk about this rank rankle OPG system. And the reason why is OPG system. And the reason why is because it's involved in bone. It's because it's involved in bone. It's involved in the immune system. It's involved in the immune system. It's involved in skeletal muscle, cardiac involved in skeletal muscle, cardiac muscle, smooth muscle. It's the most muscle, smooth muscle. It's the most prominent molecular pathway that links prominent molecular pathway that links osteoporosis and cardiovascular disease.

osteoporosis and cardiovascular disease. And it involves that protein rankle. And And it involves that protein rankle. And that signals osteoclastic activity. And that signals osteoclastic activity. And it also causes inflammation in blood it also causes inflammation in blood vessels and converts vessels and converts vascular smooth muscle cells in those vascular smooth muscle cells in those blood vessels to turn into, and this is blood vessels to turn into, and this is amazing, it's called amazing, it's called transdifferentiation.

transdifferentiation. transdifferentiation. The process is called that. And what it The process is called that. And what it does is it when you have high rankle, it does is it when you have high rankle, it actually changes those actually changes those vascular smooth muscle cells and makes vascular smooth muscle cells and makes them turn into osteoblast-like cells, them turn into osteoblast-like cells, causing them to calcify plaque within causing them to calcify plaque within the arterial walls.

the arterial walls. >> Okay. >> Okay. >> Okay. >> Now, the next slide's going to show us >> Now, the next slide's going to show us that little how it works. So, in that little how it works. So, in osteoporosis on the left here, we have osteoporosis on the left here, we have the big cell on the left is is a the big cell on the left is is a osteoblast. And then the in the upper osteoblast. And then the in the upper left, that's a a pre-osteoclast.

left, that's a a pre-osteoclast. So, the the blast have that RANKL, So, the the blast have that RANKL, that's the the ligand RANKL, and it will that's the the ligand RANKL, and it will then then then deform into that RANK receptor, deform into that RANK receptor, deforming it, stimulating those deforming it, stimulating those osteoclast, those pre-osteoclast, to osteoclast, those pre-osteoclast, to differentiate into a mature osteoclast, differentiate into a mature osteoclast, and then they form they break down bone.

and then they form they break down bone. That OPG is really important. That See That OPG is really important. That See that OPG? That's called osteoprotegerin, that OPG? That's called osteoprotegerin, and that's a soluble decoy receptor that and that's a soluble decoy receptor that shields the RANKL ligand from shields the RANKL ligand from activating that RANK receptor. So, the activating that RANK receptor. So, the more OPG you have, the less osteoclastic more OPG you have, the less osteoclastic activity you're going to have.

activity you're going to have. And on the right side, in a blood And on the right side, in a blood vessel, damaged blood vessels start vessel, damaged blood vessels start producing too much RANKL. Normally, the producing too much RANKL. Normally, the blood vessel produces a lot of OPG, a blood vessel produces a lot of OPG, a lot of osteoprotegerin, which helps lot of osteoprotegerin, which helps prevent calcification. But when blood prevent calcification. But when blood vessels are stressed and damaged by vessels are stressed and damaged by inflammation, oxidative stress, the high inflammation, oxidative stress, the high blood sugars we talked about earlier, blood sugars we talked about earlier, metabolic health, that blood sugar is is metabolic health, that blood sugar is is is deadly to vessel walls. Both the is deadly to vessel walls. Both the endothelial cell walls cells lining that endothelial cell walls cells lining that blood vessel, and the vascular smooth blood vessel, and the vascular smooth muscle cells, they start producing less muscle cells, they start producing less osteoprotegerin and more RANKL. So, when osteoprotegerin and more RANKL. So, when a woman goes through menopause, or a man a woman goes through menopause, or a man has low testosterone, or a person is has low testosterone, or a person

is under high stress and increased under high stress and increased cortisol, or they're taking prednisone, cortisol, or they're taking prednisone, or they have elevated levels of or they have elevated levels of parathyroid hormone cuz they have a a parathyroid hormone cuz they have a a para- a benign parathyroid adenoma in para- a benign parathyroid adenoma in their in their throat in their their in their throat in their parathyroid glands. All these lower parathyroid glands. All these lower osteoprotegerin. So, all of these allow osteoprotegerin. So, all of these allow more RANKL to stimulate RANK through more RANKL to stimulate RANK through which which which turns into osteoclast, which breaks down turns into osteoclast, which breaks down bone, which also causes a bone, which also causes a transdifferentiation of those vessel transdifferentiation of those vessel smooth smooth smooth uh muscle cells and converting them into uh muscle cells and converting them into osteoblast-like cells that calcify the osteoblast-like cells that calcify the plaque that's there.

plaque that's there. It's an amazing system. So, the next It's an amazing system. So, the next slide, please. So, this is one of my slide, please.

## Other labs to look at for bone and cardiovascular health

So, this is one of my favorite $5, $6 tests. This is CBC. I'm favorite $5, $6 tests. This is CBC. I'm I'm not going to talk about all these. I'm not going to talk about all these.

In my book, I I talk about the RBCs, the In my book, I I talk about the RBCs, the mean platelet volume, the mean platelet volume, the uh the neutrophil-lymphocyte ratio, and uh the neutrophil-lymphocyte ratio, and all that. So, I'm not going to I don't all that. So, I'm not going to I don't have time to go through that, but you have time to go through that, but you can go to the book and and read about can go to the book and and read about them and how important they are in in them and how important they are in in giving us an insight into what's going giving us an insight into what's going on. But, I want to talk about the red on. But, I want to talk about the red blood cells because that's one of the blood cells because that's one of the most important. And a low count, yes, most important. And a low count, yes, might be from anemia, but also might be might be from anemia, but also might be from a buildup of fat in the bone from a buildup of fat in the bone marrow. Even if a person's skinny, they marrow. Even if a person's skinny, they might have fat in their bone marrow.

might have fat in their bone marrow. So, aging, systemic inflammation, So, aging, systemic inflammation, oxidized LDLs, loss of estrogen, as I oxidized LDLs, loss of estrogen, as I said before, that can derail the said before, that can derail the development of the stem cells in bone development of the stem cells in bone marrow away from forming into marrow away from forming into osteoblasts and towards develop into fat osteoblasts and towards develop into fat cells. And the fat cells then crowd out cells. And the fat cells then crowd out another stem cell another stem cell that should be producing red blood that should be producing red blood cells, but because the fat is there, cells, but because the fat is there, then we don't have this red blood cell then we don't have this red blood cell connect formation. So, the fat is in the connect formation. So, the fat is in the form much of it is in the form of form much of it is in the form of saturated palmitic acid, which is saturated palmitic acid, which is poisonous to stem cells, poisonous to stem cells, and causes even more inflammation and and causes even more inflammation and cell damage. So, cell damage. So, how do you get rid of that palmitic how do you get rid of that palmitic acid? Vitamin D, eating like avocados acid? Vitamin D, eating like avocados and olive oil for the oleic acid and the and olive oil for the oleic acid and the phenolitic compounds, fish oil. I know a phenolitic compounds, fish oil. I know a lot of people now are taking gamma and lot of people now are taking gamma and delta tocotrienols, which is a great delta tocotrienols, which is a great product. And then for women, going on product. And then for women, going on HRT, re- keeping that estradiol level HRT, re- keeping that estradiol level high, that will help decrease the high, that will help decrease the toxicity, decrease the the fat in their toxicity, decrease the the fat in their in their bone marrow, reduce this in their bone marrow, reduce this inflammation, and improves red blood inflammation, and improves red blood cell count. So, cell count. So, when I was first diagnosed with when I was first diagnosed with osteoporosis, osteoporosis, osteoporosis, if you go to the next slide, you're if you go to the next slide, you're going to see the bone biopsy of me on going to see the bone biopsy of me on the right and a normal bone biopsy on the right and a normal bone biopsy on the left. So, the at the top of the the left. So, the at the top of the slide on the right is the outer part of slide on the right is the outer part of my iliac crest and the the bottom part my iliac crest and the the bottom part there is the inner inner cortex. You can there is the inner inner cortex. You can see how thin thin that is and how few see how thin thin that is and how few trabeculae there are in there compared

trabeculae there are in there compared to the the normal bone biopsy on the to the the normal bone biopsy on the left. And what I want to show here is left. And what I want to show here is not just that there's not many not just that there's not many trabeculae, so not much strength there.

trabeculae, so not much strength there. Trabeculae are those little squiggly Trabeculae are those little squiggly lines in the in the inside of the bone.

lines in the in the inside of the bone. But, if you go to the next slide, you're But, if you go to the next slide, you're going to see on the left of that slide going to see on the left of that slide all those white round circles, that's all those white round circles, that's fat. So, I'm pretty skinny. I'm 150 lb, fat. So, I'm pretty skinny. I'm 150 lb, almost 6 ft, and I don't have much fat almost 6 ft, and I don't have much fat on me, about 6 and 1/2 7% fat. But, my on me, about 6 and 1/2 7% fat. But, my bone marrow was completely not bone marrow was completely not completely, but it was very filled with completely, but it was very filled with fat.

fat. fat. And my red blood cell count was a 3.9 to And my red blood cell count was a 3.9 to 4.0, or a 3.9 to 4.0. So, I had a lot of 4.0, or a 3.9 to 4.0. So, I had a lot of fat in my bone marrow. The next couple fat in my bone marrow. The next couple slides is just showing that I also had slides is just showing that I also had this what's called intermittent this what's called intermittent deposition of bone. I would lay down deposition of bone. I would lay down bone matrix and calcify it, and then I bone matrix and calcify it, and then I then the next layer of bone did not then the next layer of bone did not calcify. So, those are just closer views calcify. So, those are just closer views of that. Probably genetic issue. Okay, of that. Probably genetic issue.

## Inflammation, metabolism, and cardiovascular risk

Okay, go to the next slide of inflammation go to the next slide of inflammation oxidative stress markers. We always talk oxidative stress markers. We always talk about about about inflammation. How do you tell a person inflammation. How do you tell a person has a chronic systemic inflammation?

has a chronic systemic inflammation? It's very difficult. There's no way It's very difficult. There's no way anybody can just look at a person and anybody can just look at a person and say, "You have chronic systemic say, "You have chronic systemic inflammation." We have some tests, but inflammation." We have some tests, but they help, but they're not definitive.

they help, but they're not definitive. You would think that if you have You would think that if you have systemic inflammation, everybody's high systemic inflammation, everybody's high sensitivity C-reactive protein would be sensitivity C-reactive protein would be elevated, but that's not true. But, elevated, but that's not true. But, these markers do help. As you can see these markers do help. As you can see under that HS-CRP, under that HS-CRP, greater than 2.4, you have a 30% to 60% greater than 2.4, you have a 30% to 60% greater risk of cardiovascular disease.

greater risk of cardiovascular disease. And it's above two, you have a 23% And it's above two, you have a 23% increase increased risk of low bone increase increased risk of low bone mineral density. So, all these things mineral density. So, all these things can help us look at cardiovascular and can help us look at cardiovascular and skeletal health risk. Okay, next slide.

skeletal health risk. Okay, next slide. Estrogen, as I said before, is so Estrogen, as I said before, is so important. So, when a woman goes through important. So, when a woman goes through menopause, they lose that estrogen, it menopause, they lose that estrogen, it can really disrupt the whole immune can really disrupt the whole immune system and the whole bone remodeling system and the whole bone remodeling system. Estrogen helps us decrease system. Estrogen helps us decrease osteoclastic activity. It decreases osteoclastic activity. It decreases oxidative stress. It protects our oxidative stress. It protects our endothelial glycocalyx, and we're going endothelial glycocalyx, and we're going to see what the endothelial glycocalyx to see what the endothelial glycocalyx does and why, and it's really cool. So, does and why, and it's really cool. So, if you haven't heard of endothelial if you haven't heard of endothelial glycocalyx, look it up on the internet glycocalyx, look it up on the internet cuz it's really fascinating.

cuz it's really fascinating. Estrogen also helps us lower LDL Estrogen also helps us lower LDL cholesterol, relaxes blood vessels, so cholesterol, relaxes blood vessels, so it increases nitric oxide. Nitric it increases nitric oxide. Nitric oxide's produced by that endothelial oxide's produced by that endothelial glycocalyx. Okay, metabolic evaluation, glycocalyx.

## Gut-bone-cardiovascular axis

Okay, metabolic evaluation, I've already talked about that, how I've already talked about that, how important that is, that we don't just important that is, that we don't just look at the person's lipids, but we look look at the person's lipids, but we look at their how their body deals with at their how their body deals with glucose. Okay, this next slide is about glucose. Okay, this next slide is about the gut bone cardiovascular axis.

the gut bone cardiovascular axis. And as I mentioned before, everybody And as I mentioned before, everybody should really if you have a gut issue, should really if you have a gut issue, bloating, constipation, diarrhea, I use bloating, constipation, diarrhea, I use a lab test called from diagnostic a lab test called from diagnostic solutions called the GI map which I like solutions called the GI map which I like a lot but there's a lot of companies a lot but there's a lot of companies that have other stool tests that are that have other stool tests that are very very good and can help physicians very very good and can help physicians look at the health or ill health of a look at the health or ill health of a person's gut person's gut and it's really important to assess that and it's really important to assess that if a person has gut involvement, they if a person has gut involvement, they can easily increase their risk for can easily increase their risk for osteoporosis and cardiovascular issues.

osteoporosis and cardiovascular issues. Okay, just want to talk about this one Okay, just want to talk about this one thing is called TMAO. It's a byproduct thing is called TMAO. It's a byproduct of your gut bacteria and if you know, of your gut bacteria and if you know, I'm not saying everybody should be I'm not saying everybody should be tested for this but with change hers was tested for this but with change hers was high so I'm putting it here. It high so I'm putting it here. It increases inflammation, it increases increases inflammation, it increases osteoclastic activity, decreases blastic osteoclastic activity, decreases blastic activity. It damages that endothelial activity. It damages that endothelial glycocalyx so has lowered nitric oxide glycocalyx so has lowered nitric oxide production. So all those things are production. So all those things are important so we looked at that. We also important so we looked at that. We also looked at her ADMA.

looked at her ADMA. This is a really cool little simple test This is a really cool little simple test blood test to get and it's a blood test to get and it's a it's a it's a nice blood test for preclinical nice blood test for preclinical cardiovascular disease.

cardiovascular disease. We'll go through that quickly but but We'll go through that quickly but but the reason why that's important is the reason why that's important is because if that's high, it can indicate because if that's high, it can indicate that yeah that yeah this person has cardiovascular risk and this person has cardiovascular risk and then we have to look closer and see then we have to look closer and see what's going on. Here's that endothelial what's going on. Here's that endothelial glycocalyx that I talked about. It's a glycocalyx that I talked about. It's a thin carbohydrate rich layer that lines thin carbohydrate rich layer that lines the inside of your blood vessels. It the inside of your blood vessels. It senses the blood flow. So as that senses the blood flow. So as that blood's pulsing through your arteries, blood's pulsing through your arteries, your your arterioles, it it senses that your your arterioles, it it senses that blood flow and then it stimulates the blood flow and then it stimulates the cells that line that vessel to produce cells that line that vessel to produce nitric oxide. And nitric oxide is what nitric oxide. And nitric oxide is what allows vessels to contract and relax and allows vessels to contract and relax and and uh maintains the health of that and uh maintains the health of that vessel wall. If you have damaged vessel wall. If you have damaged endothelial glycocalyx, endothelial glycocalyx, it allows for an increase in it allows for an increase in inflammation, oxidative stress, and inflammation, oxidative stress, and allows adhesion molecules to form, and allows adhesion molecules to form, and so white blood cells can attach that so white blood cells can attach that wall and then increase plaque formation wall and then increase plaque formation in the wall itself. And the interesting in the wall itself. And the interesting thing is people know a lot about the thing is people know a lot about the endothelial glycocalyx now. A lot of endothelial glycocalyx now. A lot of people have heard about it, people have heard about it, but they haven't heard of the next but they haven't heard of the next slide. And that is in bone. There's this slide.

And that is in bone. There's this exactly Well, not exactly, but a very exactly Well, not exactly, but a very similar system there. We have a similar system there. We have a glycocalyx in the osteocyte dendrites.

glycocalyx in the osteocyte dendrites. So, we have as I mentioned before, the So, we have as I mentioned before, the osteocyte is the cell that monitors the osteocyte is the cell that monitors the actions of and regulates the actions of actions of and regulates the actions of blasts and class, and they have little blasts and class, and they have little dendrites that go between them, and dendrites that go between them, and there is a glycocalyx in that there is a glycocalyx in that dendrite.

dendrite. dendrite. So, if you have endothelial glycocalyx So, if you have endothelial glycocalyx damage, you're probably going to have damage, you're probably going to have osteocyte glycocalyx damage, too.

osteocyte glycocalyx damage, too. Osteoclasts aren't going to be able to Osteoclasts aren't going to be able to talk to each other well, and now you're talk to each other well, and now you're going to have a disruption of bone going to have a disruption of bone remodeling. Okay, so Jane, let's look at remodeling. Okay, so Jane, let's look at the Let's quickly at her picture. She the Let's quickly at her picture. She had a high carb diet, and that was one had a high carb diet, and that was one of her major downfalls. It of her major downfalls. It promoted arterial wall injury and made promoted arterial wall injury and made her high lipids now get into those walls her high lipids now get into those walls causing plaque. There's no doubt about causing plaque. There's no doubt about it, she had endothelial glycocalyx it, she had endothelial glycocalyx dysfunction. She had exercise-induced dysfunction. She had exercise-induced high blood pressure and her ADMA was high blood pressure and her ADMA was high. So, she had inflammatory markers high. So, she had inflammatory markers that were high. Her blood glucose was on that were high. Her blood glucose was on the verge of pre-diabetes.

the verge of pre-diabetes. So, she clearly had issues. So, these So, she clearly had issues.

## Sample treatment plan to support bone and cardiovascular health

So, these are some of the things we did. She was are some of the things we did. She was put on a statin, as you know, put on a statin, as you know, rosuvastatin. And that has rosuvastatin. And that has [clears throat] pleiotropic effects. It [clears throat] pleiotropic effects. It does a lot of things. It doesn't just does a lot of things. It doesn't just Statins don't just lower LDLs. They help Statins don't just lower LDLs. They help increase a little bit HDLs. They lower increase a little bit HDLs. They lower interleukin 6. They increase actually interleukin 6. They increase actually bone morphogenetic protein for for more bone morphogenetic protein for for more more bone formation. Not all the statins more bone formation. Not all the statins do, but at least the lipophilic ones do, do, but at least the lipophilic ones do, the the ones like atorvastatin and the the ones like atorvastatin and simvastatin. Not that I think that simvastatin. Not that I think that they're better. I actually like they're better. I actually like rosuvastatin better, but that's a rosuvastatin better, but that's a different story.

different story. We can talk about later. But, she was We can talk about later. But, she was put on a statin and I suggested other put on a statin and I suggested other things such as TUDCA and selenium. The things such as TUDCA and selenium. The that they can help reduce mitochondrial that they can help reduce mitochondrial reactive oxygen species and reduce reactive oxygen species and reduce endoplasmic endoplasmic endoplasmic reticulum stress, which is Remember that reticulum stress, which is Remember that endopla- plasmic reticulum helps you endopla- plasmic reticulum helps you make proteins. And when there's stress, make proteins. And when there's stress, you're going to have misfolded proteins you're going to have misfolded proteins and that's not good. So, we want to and that's not good. So, we want to decrease the the you know, any stress decrease the the you know, any stress reactive oxygen species stress, any reactive oxygen species stress, any inflammation in your body that is going inflammation in your body that is going to help improve a person's health.

to help improve a person's health. Taking CoQ10 and atom E, those are all Taking CoQ10 and atom E, those are all important. I I suggested to her important. I I suggested to her nattokinase and berberine. Those things nattokinase and berberine. Those things can help with the vessel walls. She also can help with the vessel walls. She also went on timolol and then a year of went on timolol and then a year of bisphosphonates. She also went on bisphosphonates. She also went on transdermal HRT. Remember that helped transdermal HRT. Remember that

helped lower the RANKL. It helped increase lower the RANKL. It helped increase osteoprotegerin.

osteoprotegerin. osteoprotegerin. It lowered her interleukin 6 or It lowered her interleukin 6 or inflammatory markers, so her transdermal inflammatory markers, so her transdermal HRT was a vital part of her treatment HRT was a vital part of her treatment plan. We changed her diet, for sure. We plan. We changed her diet, for sure. We decreased her sugar. We did things to decreased her sugar. We did things to improve her gut health and increase her improve her gut health and increase her nitric oxide production. Beets and, you nitric oxide production. Beets and, you know, taking the TUDCA, doing things know, taking the TUDCA, doing things like urolithin A, which is I'm a big like urolithin A, which is I'm a big proponent of urolithin A. So, and like I proponent of urolithin A. So, and like I said, we tried to do things to help said, we tried to do things to help improve her gut health. And these are improve her gut health. And these are just some of the specifics. Vitamin D just some of the specifics. Vitamin D and K. We did the V's and the and K. We did the V's and the trimethylglycine to lower homocysteine.

trimethylglycine to lower homocysteine. We gave her NMN and the urolithin A and We gave her NMN and the urolithin A and alpha lipoic acid to help with her alpha lipoic acid to help with her mitochondria support. I'm a big mitochondria support. I'm a big proponent of resveratrol and quercetin.

proponent of resveratrol and quercetin. Those were important to reduce Those were important to reduce inflammation. There's two products that inflammation. There's two products that I really like from Designs for Health I really like from Designs for Health called Vasculonox and Arterosil that called Vasculonox and Arterosil that help with that nitric oxide production help with that nitric oxide production and improvement of that endothelial and improvement of that endothelial glycocalyx. Fish oil, of course, or glycocalyx. Fish oil, of course, or I I I have most people on. And just eating have most people on. And just eating better, you know, we needed to get rid better, you know, we needed to get rid of her meat and potato diet. You know, of her meat and potato diet. You know, we had her increase her her veggies, her we had her increase her her veggies, her berries, her beets, garlic, pomegranate.

berries, her beets, garlic, pomegranate. And I had her on collagen because And I had her on collagen because collagen helps collagen helps stimulate stimulate stimulate the osteoblasts to form bone. So, the osteoblasts to form bone. So, collagen is not taken for the amino collagen is not taken for the amino acids. It's taken for the polypeptide acids. It's taken for the polypeptide chains that some of them can actually be chains that some of them can actually be absorbed intact that directly stimulate absorbed intact that directly stimulate the blast to the blast to form bone. And when a person's P1NP is form bone. And when a person's P1NP is low, that's her blastic activity, low, that's her blastic activity, remember. So, if the P1NP is low, remember. So, if the P1NP is low, collagen can help that. And, of course, collagen can help that. And, of course, probiotics because uh her gut was not probiotics because uh her gut was not doing well.

doing well. So, I know I went through those last few So, I know I went through those last few slides quickly, but at least I hope that slides quickly, but at least I hope that I gave you lots and lots to think about.

I gave you lots and lots to think about. >> Two quick questions on these slides. I >> Two quick questions on these slides. I the company, I think it's Calroy, right, the company, I think it's Calroy, right, who does the vast who does the vast and answers. All right, right, right.

and answers. All right, right, right. So, it's not So, it's not >> Oh, sorry about that. Yeah, yeah, yeah. >> Oh, sorry about that. Yeah, yeah, yeah. >> Sorry, that's okay. And the second thing >> Sorry, that's okay. And the second thing was did you want to mention about her was did you want to mention about her iron cuz that was an issue as well?

iron cuz that was an issue as well? >> Yeah, she if you know it, well, probably >> Yeah, she if you know it, well, probably people don't remember, but at the very people don't remember, but at the very beginning I showed what supplements she beginning I showed what supplements she was taking and she was taking iron. And was taking and she was taking iron. And there's this there's this condition called ferroptosis.

condition called ferroptosis. And ferroptosis is this iron-dependent And ferroptosis is this iron-dependent form of regulated cell death. form of regulated cell death.

So, it involves lipid peroxidation and So, it involves lipid peroxidation and dysregulation of causing an iron dysregulation of causing an iron overload. So, her ferritin was high, she overload. So, her ferritin was high, she had all these inflammatory issues, and had all these inflammatory issues, and so when a person has this ferroptosis, so when a person has this ferroptosis, this like I said, high iron and lipid this like I said, high iron and lipid peroxidation situation, it causes cell peroxidation situation, it causes cell structure instability. And so, if the if structure instability. And so, if the if the cell membrane is irritated, is is the cell membrane is irritated, is is dysfunctional, is damaged, good stuff dysfunctional, is damaged, good stuff leaks out and bad stuff leaks in. The leaks out and bad stuff leaks in. The person's energy production suffers and person's energy production suffers and she certainly was feeling that and the she certainly was feeling that and the cell receptors don't work as well. I you cell receptors don't work as well. I you know, the OPG Y OPG, the rank rank local know, the OPG Y OPG, the rank rank local system and other systems that were not system and other systems that were not working well in her. And it leads to the working well in her. And it leads to the increased osteoclastic activity, increased osteoclastic activity, decreased osteoblastic activity, decreased osteoblastic activity, dysregulation of the of the lipids and dysregulation of the of the lipids and damage to heart cells. So, ferroptosis damage to heart cells. So, ferroptosis is not something that we should have is not something that we should have going on, so I asked her to stop the going on, so I asked her to stop the iron supplements, at least to get that iron supplements, at least to get that started.

started. started. >> Okay. So, wow, Dr. McCormick, this was >> Okay. So, wow, Dr. McCormick, this was just fantastic and everybody listening, just fantastic and everybody listening, don't worry if you don't get all of don't worry if you don't get all of this. You can watch this. That's the this. You can watch this. That's the beautiful thing about podcast, It stays beautiful thing about podcast, It stays up there, so you can review this. But I up there, so you can review this. But I think what's your your main point? I I think what's your your main point? I I think you're me you have a few main think you're me you have a few main points that you really feel so points that you really feel so passionate to tell everybody about.

passionate to tell everybody about.

## Advocating for your health and asking for the right tests

>> I guess just number one, the awareness >> I guess just number one, the awareness that these two disorders, these two that these two disorders, these two diseases are can be comorbidities. They diseases are can be comorbidities. They are not unusual to travel together.

are not unusual to travel together. And that you need to stand up for your And that you need to stand up for your health health health and speak with your doctor about these and speak with your doctor about these things and and ask for good testing. It things and and ask for good testing. It is amazing how resistant some doctors is amazing how resistant some doctors are to getting a simply getting a CTX are to getting a simply getting a CTX and P1NP or simply getting the LP little and P1NP or simply getting the LP little A and APOB. These tests do not cost a A and APOB. These tests do not cost a lot and I'm not and I'm totally confused lot and I'm not and I'm totally confused of why a doctor would want to save an of why a doctor would want to save an insurance company, you know, $200 for insurance company, you know, $200 for not doing these tests when they're so not doing these tests when they're so important to look at. So, I guess that's important to look at. So, I guess that's my my my >> It's an important message because we >> It's an important message because we believe in digging deep and when you dig believe in digging deep and when you dig deep, that's when you get the results deep, that's when you get the results and things come up. So, share with and things come up. So, share with everybody, but you you see patients and everybody, but you you see patients and you do a lot of consults and you've you do a lot of consults and you've helped so many people in the community.

helped so many people in the community. So, tell people how they can get in So, tell people how they can get in touch with you if they want if they do touch with you if they want if they do want to work with you.

want to work with you. >> Well, my office is the called Great >> Well, my office is the called Great Bones and Education and Consulting and I Bones and Education and Consulting and I do Yeah, I do do Yeah, I do consults with with people on their bone consults with with people on their bone density.

density. density. >> Now, you've been so helpful because you >> Now, you've been so helpful because you work with where people are at and you work with where people are at and you work with their So, a lot of when people work with their So, a lot of when people are confused, oh gosh, I just don't know are confused, oh gosh, I just don't know what to do. Do I go on medication? Do I what to do. Do I go on medication? Do I not? So, I always like Dr. McCormick and not? So, I always like Dr. McCormick and you've helped them. You've really shown you've helped them. You've really shown them what the path is. Are they missing them what the path is. Are they missing any root causes? And that's what that's any root causes? And that's what that's what we believe in. We believe in this what we believe in. We believe in this type of approach and it's so effective.

type of approach and it's so effective. That's the beautiful thing. That's the beautiful thing. >> Well, what I try to do is just help a >> Well, what I try to do is just help a person understand and navigate, you person understand and navigate, you know, what's going on with their system know, what's going on with their system so that they then can go back to their so that they then can go back to their doctor cuz I can't act as their doctor doctor cuz I can't act as their doctor here. So, I am just helping them here. So, I am just helping them navigate not the system, not the medical navigate not the system, not the medical system, but navigate their health and system, but navigate their health and see what's important to see how they can see what's important to see how they can interact with their doctor to encourage interact with their doctor to encourage them to them to get the right test, to ask the right get the right test, to ask the right questions, to make sure that, you know, questions, to make sure that, you know, they are getting the optimal health that they are getting the optimal health that they if they need.

they if they need. >> Well, you're doing an incredible job and >> Well, you're doing an incredible job and I always believe and I've said this a I always believe and I've said this a million times, knowledge is power. And million times, knowledge is power. And the people listening, they want to learn the people listening, they want to learn as much as they can and it really does as much as they can and it really does pay off. So, thank you so much for pay off. So, thank you so much for joining me here today and sharing this joining me here today and sharing this really, really important information.

really, really important information. >> Thanks for having me, Marci, and and I >> Thanks for having me, Marci, and and I really appreciate being invited on to really appreciate being invited on to talk about this really important talk about this really important subject.

subject. subject. >> Thanks so much. >> Thanks so much. Wow, this was filled with so much great Wow, this was filled with so much great information and I hope you have a better information and I hope you have a better understanding now of the relationship understanding now of the relationship between bone health and heart health and between bone health and heart health and what tests you should order. All the what tests you should order. All the links will be in the show notes and I links will be in the show notes and I also wanted to mention that on September also wanted to mention that on September 8th, I'll be having a free webinar on 8th, I'll be having a free webinar on strong bones for life. We'll I'll go strong bones for life. We'll I'll go over testing, nutrition, exercise, and over testing, nutrition, exercise, and all the things you need to do for to all the things you need to do for to really be successful in an integrative really be successful in an integrative approach.

approach. approach. So, that's going to be at noon on So, that's going to be at noon on September 8th and if it's past the day, September 8th and if it's past the day, I'll be having them on a continual I'll be having them on a continual basis. So, just check the show notes for basis. So, just check the show notes for that. So, thank you so much for tuning that. So, thank you so much for tuning in and I look [music] forward to seeing in and I look [music] forward to seeing