Turning the Paradigm of Hypertension and Cardiovascular Disorders upside down. "Does the chicken come before the egg?"

Dr. Joseph M. Raffaele, M.D.
Mark Houston, M.D.

Dr. Joseph M. Raffaele, M.D.
Dr. Mark Houston graduated Phi Beta Kappa in Summa Cum Laude from Rhodes College with a BA in chemistry and math. He graduated with highest honors and the Alpha Omega Alpha honorary society distinction from Vanderbilt Medical School. He completed his medical training at the University of California in San Francisco and then to return to serve as chief resident in medicine at Vanderbilt Medical Center, where he received the Hillman Award of the Best Teacher. Dr. Houston is the director of the Hypertension Institute and Vascular Biology, medical director of the Division of Human Nutrition, and medical director of Clinical Research at the Hypertension Institute in Nashville, Tennessee. He has served as an associate clinical professor of medicine at Vanderbilt University School of Medicine. Dr. Houston has presented over 10,000 lectures, nationally and internationally, and published over 250 medical articles, scientific abstracts in peer reviewed medical journals, books, and book chapters. He has published nine books, including "The Hypertension Handbook," and his newest book, "Controlling High Blood Pressure through Nutrition, Nutritional Supplements, Lifestyle and Drugs."

Dr. Joseph M. Raffaele, M.D.
Well, it's a great pleasure to have you on the show Mark, to talk about your experience and knowledge in the field of hypertension and tie in Telomere biology into that. And I know we've had some discussions before at meetings, and I'm always fascinated to get your take on cardiovascular disease from an integrative and sort of aging standpoint. So I just like to get started by asking you how your approach integrates sort of aspects of aging Telomere biology into the diagnosis and management of hypertension and risk stratification, in your daily practice?

Mark Houston, M.D.
Yeah, George one of the major differences in what I do with integrative management of hypertension and all its sequelae of CVD is we really have started with the basics of why people become hypertensive. And we factor that in to vascular aging and how that is affected by aging in general. So as you know Sir William Osler said a man is as old as his blood vessels.

Dr. Joseph M. Raffaele, M.D.
Right.

Mark Houston, M.D.
So if you can get the vasculature healthy, then the blood pressure is gonna go down. So we have really turned this thing upside down. Most traditional hypertensive specialist or internist will look at the blood pressure and decide if I get the blood pressure down I have solved the problem of cardiovascular disease. And unfortunately that has turned out not to be the case and that's been proven in the long-term clinical trials that it's not just the blood pressure, it's what happens to the blood vessel. And so how you get there is important, what you use is important and how the nutrition or the supplement or the drug affects the arterial health is important in reducing strokes, heart attacks, heart failure and kidney disease. And when you get to the basics of what it is about the vasculature, that's so important, we were looking at endothelial dysfunction, the glycocalyx and vascular compliance or elasticity. And then what is it that affects those three things? What's the basic foundation of cardiovascular disease and hypertension. And it's three things and you've heard me preach this a long time. There's only three finite responses that the blood vessel has for all the insults that it can encounter. And there's, hundreds and thousands of these, those finite responses are inflammation, oxidative stress, and vascular immune dysfunction. So in a summary of kinda what we're gonna talk about today, we'll be turning the entire prevention, diagnosis and treatment of hypertension kinda upside down, concentrating on vascular biology, vascular health, and vascular aging, which in turn is gonna improve your overall aging and all of this feeds back into all the things that you and I talk about with aging, such as telomeres.

Dr. Joseph M. Raffaele, M.D.
Yeah I mean, I think that's a really important point. There are a lot of studies that were done that show that higher blood pressure is associated with increased cardiovascular events, strokes, etcetera But now we have a much better way, we have better ways of measuring it, I think. And that's when we've learned that, you know, certain drugs will lower blood pressure, but probably don't help like beta blockers potentially don't help necessarily with arterial elasticity might make it even a little bit stiffer and, you know, the CAFE trial showed that. And then you have, so

you want to focus on the basic pathophysiology, which I think is fantastic, it's almost in some ways, a little bit like Bredesen does in his protocol with Alzheimer's disease, you want to fix all the things that can go wrong in Alzheimer's disease. And then the brain will work better rather than, you know, giving a drug that speeds the brain up, but you're really not fixing the problem, which is causing the dysfunction in the first place. So I'd love to hear more about, you know, how you go about assessing, evaluating somebody that's different than what we do in typical internal medicine or, or hypertension specialists that attitude when we talked about the stigma core, and then you talked about endothelial dysfunction and, you know, the glycocalyx, which is, you know, really gotten to be a very interesting area. So yeah, go ahead and tell us about that.

Mark Houston, M.D.
So let's divide it up into two areas of diagnostic therapy testing. Let's talk about blood in urine tests, which almost everybody can get from any lab. So the first thing you do is if you get a hypertensive patient is let's concentrate first of all, on the blood pressure itself. And how are we going to manage that? And then the second piece would be arterial health. So a patient walks in he's hypertensive. You want to know why they're hypertensive. So there's the primary, which is usually genetic and there's secondary. So the first thing you want to do is be sure the patient doesn't have a secondary cause for hypertension. And that's really not that common, maybe five or 10% of the entire hypertensive population. And most physicians know how to do that. It's 24 hour urine's, cortisol, Catecholamines, BMAs, metanephrines making sure they don't have an adrenal tumor or pheochromocytoma and so forth. Well, that part's pretty easy. The second piece is to document that the patient really has hypertension, but also to find out what their 24 hour blood pressure monitoring is because just an office blood pressure, doesn't give you adequate information about the patient's risk, about what to do, what kind of treatments involved.

And if you're giving medications, it helps you determine when to give the medication. So we have like 10, 24 blood pressure monitors in the office, and they're always busy and they monitor not just the average blood pressure, but spikes in blood pressure, lability, nocturnal blood pressure, whether the patient has nocturnal dipping or non dipping surges in the morning, so all those things are important. And I'll just give you one example of how helpful the ABM can be. Let's suppose that you have a patient whose nocturnal blood pressure is pretty high, maybe even higher than it is during the day. And they're, they don't dip at night. They don't have a relaxation of the blood vessels. So the pressure falls. So if you knew that you would say, well, it would be better for me to give whatever, whether it's medication or something else at night to lower the nocturnal pressure. However, if you have the reverse, which is the blood pressure actually is very low at night, and there are, like to call an excessive dipper. You don't want to do that because you could actually drive the pressure too low and give them a stroke. So it is

crucial to have that information. And I really don't know how you can treat hypertension in 2021 without having a 20 hour blood pressure monitor because office reads, won't give you the clues to that. So those things, blood, urine, ABM, that gives you kind of the blood pressure piece. Okay. Now the other piece, which is extremely important is what's driving the hypertension related to the vascular system. And we have about eight or 10 tests that we do in the hypertension Institute that measure everything, arterial compliance, elasticity, augmentation index, plethysmography, endothelial function, glycocalix I mean, everything you can think of, we measure it. And when I get that information, I can pretty well tell you, at least pathophysiologically why the patient has hypertension. So for example, one machine we have is called a pulse wave velocity, and it's, it measures big, medium and small artery elasticity or arterial compliance. Almost everybody who has hypertension has very, very stiff, small arteries. Sometimes they have stiff large arteries as well. But if those small arteries are really stiff, what happens is when blood enters those arteries, they don't dilate and they will rupture or clot. And if that's in the brain, you get a stroke it's in the heart and had a heart attack. So you have to loosen up the arteries with nitric oxide boosters, glycocalyx boosters, get those things fixed quickly because that doesn't reverse as quickly with even a blood pressure medication, because sometimes the medications are good on the blood pressure pretty quick, but it takes longer to get the arterial elasticity better.

So we use a lot of compounds in the office to improve arterial elasticity. So that's, that's the large and small arteries. And we have another test that measures endothelial dysfunction. That's the EndoPAT. And then we have another one that measures what's called plethysmography. It looks, it looks at all the cardiac function. It looks at cardiac muscle, coronary artery stiffness, and other parameters, sympathetic nervous system balance so for autonomic dysfunction. And that's another whole area that feeds into the hypertension and the vascular biology as well. All that supported with, 2D echoes, carotid duplex, ultrasounds of the abdomen, renal artery. So all these things will give you a fairly comprehensive view of how is the blood pressure. Does it dip? Do you have nocturnal dipping and also what's the basis of the vascular pathology present that allows you to treat both nutraceutically with supplements or nutrition and then with drugs at the same time?

Dr. Joseph M. Raffaele, M.D.
Yeah, that's a multi-pronged approach. I mean, I have a couple of those instruments but not, but I don't have the Hypertension Institute. I'm just curious about the glycocalyx what's the, I mean, obviously for the endothelial dysfunction, you have things like Neo 40 and other blood pressure medications, but what do you use to directly treat the glycocalyx.

Mark Houston, M.D.
Right now we have a glycocalyx booster. So is it okay to mention names of companies?

Dr. Joseph M. Raffaele, M.D.
Yeah this is not CME.

Mark Houston, M.D.
Yeah, sure. Yeah, it's called Arterosil.

Dr. Joseph M. Raffaele, M.D.
Yeah I've heard of that actually.

Mark Houston, M.D.
It's made by Calroy Health, and it's very effective to improve glycocalyx. We've actually done several clinical trials with them. The first one was on hypertension and we found that the glycocalyx, Arterosil actually lowered blood pressure. And at the same time improved our arterial elasticity and endothelial dysfunction. And that was without anything else, just purely Arterosil.

Dr. Joseph M. Raffaele, M.D.
What kind of a compound is that?

Mark Houston, M.D.
It's actually, it comes from a seaweed preparation. It's got a proprietary blend. I'm not sure I know exactly what all is in it, but it's a group of amino acids and glycoproteins that are attached together and they actually go in and repair and replace any damaged glycocalyx, which is the first piece that protects the endothelial lining. So if both of those are damaged, you've got a mess. If you can repair both of them, then you restore endothelial function very well.

Dr. Joseph M. Raffaele, M.D.
And when you say measure the glycocalyx, I've seen some instruments, how do they go about doing this? It was a thickness issue or is a functional measure.

Mark Houston, M.D.
Yeah, right now it's, I would say it's a test that's evolving.

Dr. Joseph M. Raffaele, M.D.
Okay.

Mark Houston, M.D.
It's in my opinion, it's testing the glycocalyx is not quite ready for general clinical use. It's maybe research at this point, but what you measure with this particular machine that is out there is the microcirculation under the tongue.

Dr. Joseph M. Raffaele, M.D.
Really?

Mark Houston, M.D.
It's kind of a rheological assessment. And it's assuming a lot of things that if the rheology in this micro vessels is normal and the red cells aren't sticking, that the glycocalyx and the endothelial must be pretty healthy, but you know, is that the case for sure? The other factors and how do you quantitate how much damage there is. I still want to hold off from recommending any glycocalyx testing directly. You can get indirect testing by using the machines that we talked about earlier.

Dr. Joseph M. Raffaele, M.D.
Well you know that the glycocalyx is involved, presuming this works through the glycocalyx because you've got the lowering of the blood pressure, the pulse wave velocity, and the augmentation index. So, I mean, you could follow those. So that might be one of the earlier things you do, because I understand that the glycocalyx is one of the earliest things to start to dysfunction.

Mark Houston, M.D.
Exactly, yeah.

Dr. Joseph M. Raffaele, M.D.
Do you do that? I mean I don't know how many people you see that don't actually have hypertension in your in your practice. Probably not that many.

Mark Houston, M.D.
Not that many now.

Dr. Joseph M. Raffaele, M.D.
But you know, it's a continuum, right? Arterial aging, hypertension has just accelerated arterial aging, essential hypertension. And so, I'd be interested for me, but also for our listeners to get, should we be testing? Is there an optimal level of these, of these instruments, the output from these instruments that we want to keep way before you actually get over 135/90. The target is right now, it's actually is 120/80 we've gotten it to, which is smart at this point. Yeah, because I do that in my practice. I want to, not only prevent hypertension, I want to keep your arteries at a 20 to 25 year old level, which I have patients who on the augmentation index, they're at 20 years old and they're 50, but they are doing all the things right. You know, they're running, they're keeping the body fat down or they're, all the inflammation is down. So that's kind of where I see it. What you do is sort of, it's a continuum. And I try to put that in my practice. So you're using Arterosil and then obviously you're prescribing exercise, et cetera. What's the next sort of step to level on that in terms of--

Mark Houston, M.D.
You hit on a very important point, and that is the chicken and the egg concept for hypertension vascular disease. And what is very clear now and pretty well proven is the arterial disease, particularly in a central or genetic hypertension, the endothelial dysfunction, and in particular, the glycocalyx dysfunction, the stiff artery loss of compliance actually precedes hypertension by decades. And so what we have found, if we get, say a 20 year old kid in the office and both of his parents have hypertension, but he's 120/80 and he thinks he's fine. We find distinct abnormalities in most all of the testing I just mentioned. His arteries are already getting stiff. His echo may show left ventricular hypertrophy or diastolic dysfunction. You know, he's already got vascular problems. So the way I think about this is the vascular disease comes first. The hypertension becomes a marker of a sick artery, and that's what happens, you know, 10, 15, 20 years later. So the beauty of this and knowing it is you can actually preempt these patients from getting hypertension by aggressively treating them with things that improve their arterial function and health, slows down their vascular aging, and either stop or delay, or if they get it, it's not as severe as it would be otherwise.

Dr. Joseph M. Raffaele, M.D.
Yeah, and that's healthcare, not disease care.

Mark Houston, M.D.
Yeah, right.

Dr. Joseph M. Raffaele, M.D.
Maintaining the health of your arteries. It's unfortunate that the large societies are not looking at it that way yet. They're still looking for arbitrary, really not arbitrary, but cutoffs, that don't make that much sense. I was interested, and the glycocalyx is obviously made of glycans and I was talking to Gordon Laos. Who's the one of the big glycobiologists. He has the glycan age test. And he was talking about a study where they looked at glycan age seems to proceed by years of he development of metabolic disease, like hypertension, diabetes. And so that goes right along with this dysfunction of the glycocalyx and this is just the IGG glycans not the actual glycocalyx itself. So it's really great that we have these tools now and this understanding of this pathophysiology to intervene at a time when it really makes the most sense.

Mark Houston, M.D.
Yeah. And the people that come in and you find this abnormality they're so delighted, number one, you found it. And number two, they realized that maybe I can avoid taking drug therapy by doing all the natural things, nutrition and taking nitric oxide boosters, like Neo 40 or glycocalyx boosters like Arterosil. And those two together by the way, are very, very powerful to reverse arterial compliance issues.

Dr. Joseph M. Raffaele, M.D.
Yeah. I see. I haven't started using, but I'm going to start using Arterosil but I see no side effects with Neo 40 really. Are there any potential side effects with Arterosil?

Mark Houston, M.D.
No. I've seen virtually nothing with either of those rarely Neo 40 people have secret citric acid problems. They get a little irritation in their mouth.

Dr. Joseph M. Raffaele, M.D.
Maybe a little.

Mark Houston, M.D.
But Arterosil, I haven't had anybody have any issues with it

Dr. Joseph M. Raffaele, M.D.
So I know that there's a large, well large, I think it was 400 direct studies I saw and I've read a number of the, sort of more seminal ones, linking telomere attrition, and Telomere length with hypertension. And I'm sure that's an area that you're interested in and know about, maybe talk a little bit about that.

Mark Houston, M.D.
Yeah, you're exactly right. Telomere attrition rate, very short telomeres, correlate with all all the vascular issues, all of them, whether it's hypertension, stroke, coronary heart disease, aneurysms, all those things are part of the shortening of the telomere, which makes sense if you think about it, it goes right to the very initial premise that we talked about, which is hypertension really is accelerated vascular aging. And if your arteries are showing aging, they're gonna, you know, be associated with short telomeres.

Dr. Joseph M. Raffaele, M.D.
Yeah the question is, is it an association or is it potentially causal?

Mark Houston, M.D.
That's a great question.

Dr. Joseph M. Raffaele, M.D.
Yeah. Because then would something like TA 65 help in the same way that Arterosil does with helping the glycocalyx would that help put off either, you know, hypertension or cardiovascular disease, coronary heart disease atherosclerosis through the third area, which you mentioned potentially affecting immune dysfunction within the arterial vasculature.

Mark Houston, M.D.
Yeah, I think it's really a bi-directional issue. And I'll give you the reasons I think that. In other words, short telomeres increase vascular aging and vascular aging shorten your telomeres quicker. So--

Dr. Joseph M. Raffaele, M.D.
Yeah it's probably--

Mark Houston, M.D.
Lets just take one example.

Dr. Joseph M. Raffaele, M.D.
I'm sorry I'm having trouble here with my computer. Give me one second. It's turned my screen off and trying to fix that. We just haven't figured out yet, so I can't see you until I do this. Okay you're back.

Mark Houston, M.D.
All right. So here here's an example, but you know, as I do that, there's a lot of things that shorten telomeres. But if you look at the three finite responses that I mentioned earlier, all three of those shortened telomeres, okay. So if you're at a high oxidative stress or inflammation status, which most hypertensives are, their telomeres are gonna shorten. So as the telomeres shorten, then the blood vessel gets unhealthy quicker, which then feeds back into more hypertension. So that's why I really think it's a bi-directional loop with these things. So the comments you made, which are, if we can increase telomere length by different mechanisms, improve the vascular aging by different mechanisms, we stop that bi-directional feedback loop.

Dr. Joseph M. Raffaele, M.D.
Yeah, I was curious to see, or to read in the reanalysis of the WOSCOPS trial, where they looked at using statins to prevent coronary heart disease in the individuals who had longer telomeres the status didn't really have an effect because they didn't need to. The vasculature was already healthy. LDL might've been getting oxidized, but was able to repair itself. And that I thought was another way in which is tied in, I mean, there's other association, observational studies looking at telomere length and risk of cardiovascular disease that, taking age out of it, and other risk factors still there is a pretty big, I think odds ratio of 1.4, 1.5 for the shortest third versus the longest third of that. So keeping your telomeres long, do you think that figures into who gets essential hypertension, has anybody looked at, to your knowledge, whether families with essential hypertension might have shorter telomeres?

Mark Houston, M.D.
I have not seen that data. That doesn't mean it doesn't exist. It makes sense though, that if you did a group of a telomeres in normals versus hypertensive, you could easily see a big difference in telomere length. I'll look into that. I think it's a great question. And there may be some studies out there that have actually done that. I just don't know.

Dr. Joseph M. Raffaele, M.D.
That would be hard to know. As you've mentioned, it's a there's bi-directional feedback. I mean if you have hypertension, you might be causing more oxidative stress and shortening your telomeres, so vice versa. I'm sure you're aware of probably the tactic trial where they're looking at using TA65 in people who've had an MI within the past six months, angiographically proven atherosclerosis and seeing if a year of TA 65 reduces recurrent MI's and through reducing immunosenescence. So maybe you could talk a little bit more about the sort of mechanics of the immune dysfunction and the kind of inflammation that we see in, in hypertension as that third response.

Mark Houston, M.D.
Yeah, we use three different labs, actually four labs that measure all the inflammatory and oxidative stress parameters and also immune dysfunction. And I'll just mention those because I think you will help your audience. We use a Cleveland heart lab, which has a great immune inflammation panel. We use a PULS, which is out of California. We use Chorus, which looks at obstructive coronary heart disease. And the newest one we're using is Provincial, which I just learned about about three weeks ago, which is a extremely well validated testing for arterial health and coronary heart disease. They all measure different things. And so you can have one that's abnormal and the other three normal, but because they're measuring different things, you get a really good composite picture of what's going on with your patient. For example, inflammation markers, oxidative stress markers, and immune markers can be present, but they don't yet have a functional or anatomical problem with a disease, they're just early on. Then the next test, which is PULS, it also is a functional test. It measures inflammatory markers and growth factors in the heart muscle, that predicts the five-year risk for myocardial infarction. Now, once again, because it's functional, it doesn't necessarily mean you've got obstructive plaque, but it means that if you don't get those things fixed, you're going to progress to plaque or some set of arterial nonobstructive dysfunction, have a heart attack. Within five years?

Dr. Joseph M. Raffaele, M.D.
Oh, that's interesting. So this is molecules that are released from the heart muscle, you said?

Mark Houston, M.D.
Yeah, it's interleukin 16. And then there's a bunch of others that are called EO techs and FAS. They have very strange names that most people have never heard of, but it's well validated. Doug Herrington in California developed this particular test. And, and we've probably done, I don't know, 2000 or 3000 of these tests over the last several years and really have some validated information correlating with other things.

Dr. Joseph M. Raffaele, M.D.
And so the usual treatments that you were talking about address, or is there a specific way to address the inflammation?

Mark Houston, M.D.
Yes, there is. We have developed a treatment protocol for the PLS test based on the markers. And most everything is supplements. plant-based diet, nutrition and occasionally a drug that treats the different markers. And if people follow the regimen, they do have their markers come down. It may take a while. It may take four months, six months or longer, but almost all the patients do have improvement in their functional markers.

Dr. Joseph M. Raffaele, M.D.
What would be some, like the top three supplements that you might employ?

Mark Houston, M.D.
Let's see, we use a lot of Curcumin, Coresatin, Omega 3 fatty acids, Resveratrol. And one of the drugs we use is an ARB, like Micardis for example.

Dr. Joseph M. Raffaele, M.D.
Oh, okay sure.

Mark Houston, M.D.
Which has some really good effects.

Dr. Joseph M. Raffaele, M.D.
So Micardis will reduce these inflammatory cytokines.

Mark Houston, M.D.
Yes. It's through the blockade of the AT1 receptor, which cuts off the oxidative stress inflammatory pathway.

Dr. Joseph M. Raffaele, M.D.
Yeah, I've always talked to patients. I mean, when they're worried about taking an ACE or an ARB, It's, I don't wanna take a drug. I mean, it's almost like if you choose the right one, these are almost vitamins for your, for your arterial system. Cause you're really getting at the root of the problem not just lowering blood pressure, lowering blood pressure is a side effect. And exactly what you're talking about, they're reducing the inflammatory and the inflammation. And once I explain it to them that way they're they're more willing to use it. Would you, even in the absence of hypertension, if you couldn't get, and maybe you, always do get, but get enough of a reduction in these early markers. Would you add a Micardis or an or an ACE inhibitor or something like that even before hypertension?

Mark Houston, M.D.
Yeah, I'll tell you a big secret that a lot of people don't know ARBs and ACE inhibitors are anti-aging drugs.

Dr. Joseph M. Raffaele, M.D.
Yeah, I mean I've always--

Mark Houston, M.D.
You know that, but most people don't.

Dr. Joseph M. Raffaele, M.D.
I think you're absolutely right.

Mark Houston, M.D.
And Metformin is probably an anti-aging drug as well.

Dr. Joseph M. Raffaele, M.D.
I mean, well, Nir Barzilai is going to try to prove that with the TAME trial.

Mark Houston, M.D.
Yeah hopefully. But I found out about ACEs and ARBs in 2003 at a COSEG meeting, it was a researcher from Puerto Rico who'd done it in mouse models and he slowed down the aging in mice by 30 to 40% with ACEs. It was unbelievable. So I said, well, I'm not waiting for a human study, which will never happen. So I started taking Micardis, whenever it came out, I started an ACE or an ARB early on. I've been on one of those since 2003. And I, you know, I'm kind of a self Guinea pig. I check my telomeres and all these other tests. And I really think that it's slowed down aging dramatically in me, and I've done it in other patients and seen the same results. So the answer to your question is, yeah, I use a lot of ACEs and ARBs in people who don't have hypertension for other reasons for vascular health and/or vascular aging.

Dr. Joseph M. Raffaele, M.D.
I mean, I think that is probably going to be the future. I've toyed with the idea of Micardis you know, we use comes off of the, the augmentation pressure and new augmentation index on the stigma core instrument, was always in the, you know, 20, 25 year old range and less exercise lately, I mean hopefully I can get it back, but I'm going to be 62. So maybe I don't have hypertension, but I'm thinking about getting started on one of those, either an ARB or an ACE, depending on, you know, if I get a cough to the ACE and I can't do that, but so you're using Micardis then in yourself?

Mark Houston, M.D.
Yeah.

Dr. Joseph M. Raffaele, M.D.
Yeah, so and is it a lower dose? You just, you have to--

Mark Houston, M.D.
You have to start low, unless you've got high blood pressure and cause you'll get some hypotension. So what I did, I started it like 10 milligrams and take it right before I went to bed. So I wouldn't get dizzy. And then I worked my way up and eventually I was able to tolerate a 40 milligram dose and we don't really know how much you need in a human to do all these things. But 40 milligrams of Micardis a day is a pretty good dose to take.

Dr. Joseph M. Raffaele, M.D.
With really no side effects, but probably, people talk about lowering blood pressure causing problems with erectile function probably the opposite, probably helping them.

Mark Houston, M.D.
It actually, Micardis increases nitric oxide levels and probably helps ED. And once you kind of get used to it in normotensive patients, it doesn't tend to lower the blood pressure very much at all.

Dr. Joseph M. Raffaele, M.D.
I'm curious about Quercitin that is kind of thought of as a Senolytic which, a weaker one, I think Fisetin's a little bit more powerful use it chronically, because some people talk about cycling it, you think it's working through acidolytic effect or more through an antioxidant effect. Do you have any thoughts about that?

Mark Houston, M.D.
Yeah Quercitin is an amazing supplement. I take it every day. I also take Biofinestine with it, which makes it even work better.

Dr. Joseph M. Raffaele, M.D.
What, Bio?

Mark Houston, M.D.
Bio Finistine.

Dr. Joseph M. Raffaele, M.D.
Huh never heard of that.

Mark Houston, M.D.
So I take 500 milligrams twice a day. It is a Senolytic no question. And it does get rid of all that stuff that ages you quicker, but it also has other effects, mass cells and prostaglandins and immune function and allergies and all other things. So it has really all the effects that we talked about. The three finite responses are probably treated with Corsatin.

Dr. Joseph M. Raffaele, M.D.
Wow, and a reason of Corsatin over Fisetin? Or just?

Mark Houston, M.D.
Yeah, together, use them together. There's a company that makes them together. I think it's called Life Extension.

Dr. Joseph M. Raffaele, M.D.
What a company.

Mark Houston, M.D.
It comes together, yeah.

Dr. Joseph M. Raffaele, M.D.
Great. So those are the top three and omega-3's of course you follow omega-3 fatty acid levels with the Cleveland heart tests. I guess they have one of those. And any thoughts about, telomere length has been associated, longer telomere is associated with higher levels of intake of omega-3 fatty acids. And of course, cardiovascular disease. I forget blanking on his name right now. I think it's Harris. That's shown that the relationship between omega-3 fatty acids levels and cardiovascular disease around the country, around the world, I mean different countries. So obviously are you in the, do you do it by measurements? Are you just to two grams a day, four grams a day?

Mark Houston, M.D.
If I'm doing prevention, I will measure their omega-3 index and try to get it at eight or so, if I'm treating a specific problem, I may push the dose higher and the Omega-3 index is going to probably go higher, but I don't get too worried about it. So the dose can be all over the place. It can be anywhere from one to five grams a day. And the studies actually show that if you're up

at around four grams a day, that has the greatest risk reduction for myocardial infarction. And there's also, this is probably a good time to dispel some myths.

Dr. Joseph M. Raffaele, M.D.
Sure.

Mark Houston, M.D.
About omega-3s that have been out there. We've had for the last four years, different companies and universities battling each other, about don't take them, take them. Which one, how much DHA versus EPA. I mean, it's all over the place.

Dr. Joseph M. Raffaele, M.D.
And then there's--

Mark Houston, M.D.
I've really looked into that very carefully and tried to skew out the bad studies link the good ones. Here's what I think I could be wrong, but I've looked at it carefully. The first issue was are omega-3s good or bad? Well, I think it's been proven now. They're definitely good. I think we that myths gone. Now what omega-3s should you take? Now we have the argument of, you need more EPA than DHA. It seems to be more biologically active. If you took too much DHA, it might counterbalance the effects of the EPA. That remains to be proven. That's a theory at this point, but some of the formulations that I did 10 years ago were mostly EPA. Cause I had talked to a lot of Omega-3 specialists. So the one that I use, which is from Biotics is two thirds EPA, and one third DHA. That's one point. The other very important point is that omega-3 fatty acids become oxidized, not only in the bottle, but in your cell membranes. And you say, well, how do I prevent that? Cause I don't want that happening. You put Gamma Delta Tocopherol in your cell membranes and in the capsule. So there's a certain dose you need for that.

And it's Gamma Delta Tocopherol. Not alpha and not beta. So you have the right dose and the right Tocopherol. And then the fourth point is when you give high doses of EPA, DHA, you deplete GLA. Most people don't know that either. And that's not good. GLA is the, least higher on the link there is a good omega-6. So the formulation with Biotics, which is EFA-sirt Supreme has all that in there in every capsule. So you just have to figure out how many you want to take and you're home free and it's good quality. Now then we have the next thing that's popped up, which is atrial fibrillation. So all these studies now are suggesting a small percentage of people on omega-3s get a-fib. Well, the question is what type of omega-3 were they taking, what was the quality? Was it balanced? How much EPA, DHA, Tocopherol, GLA was in it? So that, that whole thing about atrial fib is out there. But I think we still need to be careful about assuming

that that's a big problem til' we start saying let's really look at high quality studies with high quality omega-3s. Be sure that we're okay.

Dr. Joseph M. Raffaele, M.D.
Well you may have a bunch of fascinating points here. A couple of followup questions. The first one is about atrial fibrillation because I've been seeing more of it in my practice. I do use a lot of fish oils. I'm not aware of that study. So I'd just love to know, if just briefly, you know what the author is citation. So we can, I can look it up on pub med probably, but you know, that would be interesting to see. The other point, interesting point is from a vascular standpoint, EPA potentially could be more important, but you talked to the neurologist and also Alzheimer's people and they're like EPA is only important in so far as it gets turned into DHA. And you know, if you give too much EPA, then you might, it might mess that process up too. So, I think it's probably, they're both true maybe from an inflammatory and prostaglandin standpoint in the vasculature EPA is more important, but within the brain DHA kind of rules. So I think most fish oil omega-3 products are about, whatever it is, 60 40, something like that, EPA, DHA, you can't get one that usually has more DHA than EPA.

Mark Houston, M.D.
Right.

Dr. Joseph M. Raffaele, M.D.
So that's going to happen anyhow, but yeah, it's, it's kind of interesting. Do you have any thoughts about the SEPA versus the icosapentyl versus whether there's really any benefit. I mean, pharma wants us to think there is. So?

Mark Houston, M.D.
Well those are mostly EPA.

Dr. Joseph M. Raffaele, M.D.
Right, yeah.

Mark Houston, M.D.
But the problem is they don't have any GLA and they don't have any Tocopherol. So it's still an oxidizable form. So I don't typically prescribe those. I usually use the Biotics preparation because it's two thirds, EPA and one-third DHA, but your point is exactly right. You ask yourself the question, why am I giving the omega-3 to begin with, well, if it's for eye brain or blood pressure, DHA works better than EPA.

Dr. Joseph M. Raffaele, M.D.
Right.

Mark Houston, M.D.
But maybe for other things, EPA is better. So when I developed this and I talked to a lot of people, I said, can you tell me what's kind of in nature? I mean, if I go eat cold water fish, what do I get? They said, it's about two thirds EPA and one third DHA.

Dr. Joseph M. Raffaele, M.D.
Yeah because--

Mark Houston, M.D.
And I decided on that, that's what I'm gonna do.

Dr. Joseph M. Raffaele, M.D.
Right, yeah I think that's probably a good way. And any thoughts on krill oil? Some people talk about krill oil being better than omega-3 from fish oil. I know the concentrations are different. There's less of it in there, but they say there's some benefit to it.

Mark Houston, M.D.
Krill oil. I'm not a big fan of it because there really aren't a lot of clinical studies with krill oil for anything.

Dr. Joseph M. Raffaele, M.D.
Right.

Mark Houston, M.D.
Lipids blood pressure or CHD. That's not to say krill oil isn't good. But if you've got omega-3s that are proven, I would go with that over krill oil anytime.

Dr. Joseph M. Raffaele, M.D.
Yeah and there was a lot of people that say, well it's because it's better because they're lower in the food chain. And so there's less chance of concentrating mercury or other pollutants in it. And you know, they distill these things. There's no mercury in these.

Mark Houston, M.D.
Right. The companies take care of that.

Dr. Joseph M. Raffaele, M.D.
That's one of the myths out there. That the supplement industry is very happy to talk about. So in particular the Krill people. Well, so that's, those are really good points. I'm particularly fascinated about the ARBs that you started. In terms of what you actually do with protocols and whatnot with, with TA 65 and telomere testing. How do you approach that in your patient population?

Mark Houston, M.D.
Right, so there's one company in the US that does the PCR telomere testing and that's SpectraCell, and then the other one as you know is out of Spain and they actually measure short telomeres. And I think most of us feel that the short telomeres are really what drives the aging process rather than the average. So if you're going to do telomere testing, you can pick which one you want to, but you got to know what the difference is. And then we measure it once a year and we do all kinds of things, most of which we talked about controlling all the risk factors, TA 65, nitric oxide boosters, glycocalyx boosters, exercise, plant-based diet. And we do see improvement in telomere function over time. And it's very highly correlate with vascular aging and all the cardiovascular events.

Dr. Joseph M. Raffaele, M.D.
Yeah, I definitely see people and I've been treating people with TA 65 now for 14 years. You know, most of them don't have any loss, some have an increase in telomere length. I would give you a third option though for telomere length testing, which I think is as good or better than the other two is Repeat Diagnostics in Vancouver, Canada.

Mark Houston, M.D.
Oh good, I didn't know about that one.

Dr. Joseph M. Raffaele, M.D.
They do the same sort of flow fish type tests as Life Length in Madrid does when you mentioned which, and they're both good companies, but you get both the granule sites and the lymphocytes from repeat diagnostics, which gives you a measure of, all the slings and arrows from an oxidative stress, viral infections, psychological stress standpoint of causing shortening of the lymphocytes, but then the granular sites, which of course are the neutrophils only circulate for a day. And so you really get any reflection of the bone marrow stem cell telomere length and your inheritance. And you can see that gap largening, getting larger between the lymphocytes and the granulocytes, when you see patients that have a lot of low Alyce static load, as they call it, from infections from stress, from bad diet, from being

overweight. So I think that's pretty useful. I would also say that while PCR is great for large studies, cause you batch it, their inter-subject variability and interest temporally is pretty, it's pretty significant. So I'd take a look at Repeat Diagnostic, they do all the children's hospital's telomere length testing. And they have, I think really a good coefficient of variation around 2% to 3%.

Mark Houston, M.D.
Wow that's great, okay. I'll definitely look at that. Thanks for the information.

Dr. Joseph M. Raffaele, M.D.
So I think that, you dispelled myths, given us pearls, and your approach, is there anything more you'd like to talk to me about.

Mark Houston, M.D.
Just one other major point it's very important. When you're treating hypertension and the blood pressure is definitely elevated by the criteria we've talked about, office readings in ABM or home readings, whatever you want to use. You don't want to wait to get the pressure under control. So people will say to you, well, can I try diet and weight loss and some supplements first? And I would say I'm all for that. But here's the problem. If I wait even one month or two months, you'll never catch up and be as healthy as if I started today. So my approach is let's get you on a good drug for blood pressure, start your other lifestyle programs, get the pressure to 120/80, make sure you're dipping appropriately and all those kinds of things. And then if that's done, you can then back off later on the drug, if you're getting healthier. And that was, there's a lot of studies that have shown that. So the point I want to make is the earlier the better to normal.

Dr. Joseph M. Raffaele, M.D.
That is a really fascinating. I think a good point. I mean, that goes against what most other doctors I'm sure would do, which is to say, if it's not 180 or 200/120 they're like you have some time, you're not going to stroke out, but saying you're damaging your arteries with this high blood pressure. And you're never going to be as healthy if you wait even a month, which that's incredible, is I think a paradigm shift for some doctors that might be listening to this and most of them probably, and I, myself even who was very focused on subclinical disease, I'll have that conversation with patients. But I think, you know, you've changed my mind. I think that is the right way to go. Really, It makes the most sense.

Mark Houston, M.D.
Yeah, and patients, if you approach it that way, they won't give you too much trouble about saying, I don't want to do what you're saying. They're all for getting healthier. And then you demonstrate that it works. So they're all in.

Dr. Joseph M. Raffaele, M.D.
That's right? Like you told me you were draining their 401k when you could wait to sort of slow down the draining, but we can stop it now they'd probably say stop it now. And that's yeah, it's a biological 401k.

Mark Houston, M.D.
Yeah. The other thing I'd throw in here is when would you have a drug naive patient? We stratify their hypertension into high renin and low renin. And that's easy to get, Quest labs does it plasma renin activity and aldosterone levels in the blood. And you do them at the same time, drug naive patients and tells you which group they're in. And it tells you what drug class is going to work the best, like for high renin hypertension, ACEs, and ARBs work the best. Low renin hypertension, some of the better diuretics and calcium channel blockers work best. So that gets you straight into a quicker analysis of what you need to give them is going to work better. The other thing we're doing routinely now, and in all of our hypertension and CBD patients is genetic cardiovascular testing. And I want to give you the name of the lab that we use. It's the best in the country. It's called Vibrant V I B R A N T America, Vibrant America Labs. They're out of San Francisco. And I developed this genetic profile with them about five years ago, measures about 25 different SNPs. And I got to tell you, when you get this back, you can figure out much better what type of hypertension they have, what do you use to treat it? You've got their coronary heart disease, MI SNPs, or diabetic SNPs, or lipid SNPs. And you know exactly what to do to turn off the gene, which is called gene expression testing, which we can now measure with all those test we talked about.

Dr. Joseph M. Raffaele, M.D.
Right, right, right, exactly.

Mark Houston, M.D.
Those are things that should become routine I feel in hypertension management.

Dr. Joseph M. Raffaele, M.D.
And how about even in, because there is basically when we talk about hypertension being accelerated arterial aging, there are people who don't have hypertension when you're seeing

them at age 40, but probably will have it at 60. They have a little bit steeper trajectory towards hypertension than average arterial aging, which is making it to an 80, 90 without high blood pressure. Should we be looking to see whether they have maybe some of those SNPs? It sounds like we could.

Mark Houston, M.D.
Yeah, because what I see, because I see so many referrals, I get all the resistant hypertensives they come in on five drugs and it's just totally irrational. And I said, has anybody ever checked your genetics to see why you're hypertensive? And of course, none of them have. I get the Vibrant technology genetics on them, identify one SNP that's related to a specific drug that would work. Most of which they're not on. For example some of your listeners probably never heard of Amiloride for example.

Dr. Joseph M. Raffaele, M.D.
Oh yeah right, that's an old drug.

Mark Houston, M.D.
Well amiloride has become the new kid on the block.

Dr. Joseph M. Raffaele, M.D.
Is that right.

Mark Houston, M.D.
It blocks the sodium epithelial channel. And about 30% of people have resistant hypertension, have an upgraded sodium epithelial channel in their kidney, but also in their arteries. So their arteries are full of sodium. The body's full of sodium. Nothing works. You can give them everything you want to, but you put them on Amiloride by itself for like six or eight weeks, and the pressure comes to normal usually. You may have to give a diuretic with it for awhile, but most of the time you've replaced five drugs with one drug.

Dr. Joseph M. Raffaele, M.D.
Wow--

Mark Houston, M.D.
That's what a, the CYP 411. That's the SNP you get. And you see it, and you think oh I've got it fixed now. And then the other one is huge is a one that's related to aldosterone. These people make too much aldosterone, but they don't have primary Aldo. Okay, they look like it. But when you do their testing, you don't see these really high levels of aldosterone. There may be up a

little bit, but they're not huge, but their arteries are very sensitive to aldosterone receptors. They make too much because the aldosterone synthase gene is cranked up. So you get that SNP, you put them on Spironolactone or Eplerenone, and about six or eight weeks later, their pressure comes to normal. That counts for another 20 or 30% of resistant hypertensives

Dr. Joseph M. Raffaele, M.D.
Those are all absolute pearls. Amiloride is an old, older drug used in pregnancy right?

Mark Houston, M.D.
Oh gosh, yeah. It was, it was a made by Merck. It was a hydrochlorothiazide and Amiloride together I don't even remember the name of it, but that's where, and you could still get it, I mean by itself. And it's an incredible agent. It's very popular here in Nashville because we prescribe so much of it.

Dr. Joseph M. Raffaele, M.D.
Right. The pharmacist, they keep it in stock down.

Mark Houston, M.D.
They do, yeah.

Dr. Joseph M. Raffaele, M.D.
Sounds good. Well, listen this has been a really fascinating conversation and you know, as always, learned so many new things, whenever I go to one of your lectures and today being able to ask the questions, it's been a pleasure and an honor to have you on the show, look forward to seeing you at the next meeting. Probably a A4M or I know you're always flying around doing something, so. Thank you very much for being on the Telomere Summit.

Mark Houston, M.D.
Let me ask you one other thing if I may. Can I do the plug on the blood pressure book for us?

Dr. Joseph M. Raffaele, M.D.
Oh sure, yeah. I forgot about that, absolutely.

Mark Houston, M.D.
Yeah. So I'm going to show you the book. This is, lets see if I can get it.

Dr. Joseph M. Raffaele, M.D.
Yeah get it real close to your camera. I bought a copy on Kindle and it's a great.

Mark Houston, M.D.
So there--

Dr. Joseph M. Raffaele, M.D.
Little lower, little lower.

Mark Houston, M.D.
Is it upside down?

Dr. Joseph M. Raffaele, M.D.
No you got it, that's right, just a little lower. There you go, perfect. Controlling high blood pressure through nutrition--

Mark Houston, M.D.
So this is a published one month ago, you can get it on Amazon or most of the major bookstores, and it's got everything in it that we've talked about. Plus a whole lot more. Nutrition, supplements, lifestyle, drugs, diagnoses, treatment, testing. I mean, literally everything we've talked about is in there, it's written for both the lay public, but also for physicians. And hopefully you'll find it helpful.

Dr. Joseph M. Raffaele, M.D.
Yeah, no, I got a copy of it and it is written in a really understandable, it's laid out in a really nice way and then practical as well. So I highly recommend it. Again, great talking to you and hope we may cross paths real soon.

Mark Houston, M.D.
Appreciate your time. Thanks for the interview.