Introduction and Speaker Background

Hello? Doctor Joseph Raphael. I'm your host for the Telomere Summit. Bye, doctor. Doctor. Summit. I'm pleased to have on today Doctor Ron Rothenberg, who is a pioneer in the field of regenerative and preventative medicine.

He was among the first group of physicians to be recognized for expertise in this rapidly emerging field, and has been, recognized by the American Board Anti-Aging and Regenerative Medicine.

Doctor Rothenberg got his medical degree from Columbia College of Physicians and Surgeons in 1970, and has been practicing medicine ever since then. He was supported in emergency medicine and family medicine.

And has taught in the field for many, many years at the University of California, San Diego. Doctor Rothenberg has been involved in telomere, clinical practice and anti-aging medicine for many years.

He is well known as an educator of over 50,000 physicians over the years at various courses and conferences. He is also practicing what he preaches and is an avid, surfer, skier, mountain biker, and looks like elliptical rider.

With with that in the background there. Pleasure to have you on, Ron. Oh. Thanks. You. It's, it's an honor to be here. This is going to be a lot of fun.

Yeah. So why don't we start out? I know you and I have talked over the years, many times at conferences, and we've heard each other lecture about things.

Why don't we start out by talking about your, idea about the role of the relationship between telomeres. What we do in the rest of our practice is hormone optimization.

Looking at immune function. And then you also like to speak about, the role of environmental toxicity. Sure. Telomere is really you can look at as the central piece of everything we do, putting it all together.

So protecting telomeres, you're protecting genome instability. You're controlling oxidative stress and controlling inflammation. You know, inflammation is related to everything as we've learned more and more, you know, through the years.

So telomere science, it's right in the middle of all this. And then there's other well, I like to say connect the dots, which we can know about from environmental toxicity, lifestyle, nutrition, stress reduction.

They all come together. And so all the things we've been learning to try to keep ourselves and our patients healthy. We can say the telomere science fits right in the middle.

Yeah, that's that's absolutely true. You know, the the nine hallmarks of aging, it's number two on the list. Genomic instability being number one. I would argue that probably they they're interchangeable at the top of that list.

And everything trickles down from there. Not to use a phrase from the, from the 80s and, you know. But in a good way, it trickles down to, to understand what's going on.

And, you know, all this is documented in peer reviewed literature. It's not just a nice idea, but every step along the way has has been published independently.

And that's, you know, that's what's so important. Yeah, that's what's fascinating about it. I think I did, a look at, the publications and the exponential increase in ones that had telomeres and telomerase in them since the 90s.

And, you know, every aspect of it from molecular biology through cellular biology and then up through, you know, large cross-sectional studies looking at the relationships, it's all been tied together.

And then also many clinical trials in animal models. Some of those things we'll touch on today. Okay. Great. So why don't you give me a I know I love listening to your lectures when you sort of give that brief introduction to telomere biology.

You know why? Why it's important. And then also, what? Telomerase is the enzyme that makes them longer. Well, okay. Yeah, we can start. So again with thinking that telomere this is the centerpiece. So.

The concept of telomeres resolved a lot of mysteries in molecular biology and DNA. What was called the end replication. Problem. And going back into the 60s that Hayflick limit.

So Leonard Hayflick determined that in a skin, fibroblasts and cell culture would divide around 50 times and then stop. The mystery was where's the counter, who's who's counting?

And even some comments in his papers were, I'll leave this to future generations to determine. And then Elizabeth Blackburn and her group awarded the Nobel Prize for understanding that the telomere is the counter in our cells.

So each, division a section of telomeres loss.

Telomere Biology and Aging

That's the gtgt. And when telomeres become critically short, cell function is, impaired and is, you know, and end of the road. And so in our germ cell line, telomeres restored by the endogenous enzyme telomerase or else life would have continued through the eons.

But in our somatic cells, you know, the rest of us. So our minds and bodies, they're limited by, you know, telomere degradation, either in rabbits, especially in rapidly multiplying cells, the immune system, skin epithelial cells, but also in post.

There's a big role for this and post mitotic cells too. And this is another mystery that's been unraveled in the past few years. So this section is ended by telomerase.

And the gene for guanine is very susceptible to oxidative stress. And that is part of the connection. So this is mostly you know you got three GS there.

So oxidative stress from the mitochondria you know energy power plants turning at ATP and having its waste products. They're damaging the mitochondria and that damaging the telomeres.

So there's a vicious cycle going in and back, but it can be prevented by a feedforward cycle to to prevent this. And so we apply the telomerase again, the endogenous enzyme that can be turned on by TR 65 is the more you start learning about it, the more windows open and it gets more complex.

Right. So we are presentations. The main components of are church, telomerase turn and talk. So the third telomerase in a t RC is the RNA template that the church puts on different tags.

And so I tried to make a little ways to remember this. So t rc sounds like a turkey and it's a RNA template. And a turkey's ready in November afternoon.

I know that's silly, but that moment that way, that telomerase reverse transcriptase. But the, third is the motor that puts them on. And sometimes it's written as h tert or h start meaning human.

But a study with a mouse that could be entered or enter. So we've got these and these and these components that restore telomeres if they're turned on.

But also as we can talk about later, there's non-canonical actions. You know, the canon is like official body of knowledge for theology or, or Star Wars or in this case, in this case is, telomeres.

But let's leave that for a little bit as a little bit of a teaser for later and sort of for just a bit with the sort of the canonical, if you will, activities of telomerase, you know, the reverse transcriptase, and, and, you know, sort of it's repressed at birth.

And so people often ask, you know, when does aging begin? And some people say at about, you know, peak reproductive health, which is in their mid 20s, but from a telomere length standpoint, since alarm raised is turned down, it's really at birth.

And you start to see erosions of your telomeres, you lose them pretty rapidly going from a single cell to, you know, whatever, 13 whatever the number is trillion cells that you want.

And depending on the size of your shack or, or or, you know, tattoo, there's a differential number of cells there, but, so you lose them fairly rapidly in that growth period.

And after that, there's kind of a 50 base pair per year, a loss of telomere length. Because it's turned on but not sufficiently in the cells. So that gradual loss is what is what we're talking about with, with telomere length. And, you do that or you do some measurements of telomeres in your practice. Yes.

The, there's different methodologies, you know, that are available. We've used, the, life length, company. I've no, business, a personal relationship with them, the disclaimer who do the IQ fish test.

And so I think there's various methodologies, but it's important to use the same ones so you can follow patients. And, it's a little bit quirky to get because it has the it's a separate lab test, but, and some patients just want to dive in there.

And, you know, I try to encourage the testing, but if they don't want to, that's okay. As well as since, you know, a tradition of the many patients we've tested over the years, I'd say a few have made outstanding improvements in their telomere length.

Most have made a steady improvement, which may be plateaus at a certain point and may zig and zag. And a few have stayed about the same. But even that is, this is a victory because we know what nature has in store for us.

You know, I can see the loss of telomeres, right? We, you know, as you were saying, we've aging starts at conception. You know, it sounds kind of silly, but we lose a third of that rapid cellular division and embryogenesis, lose a third of our telomeres. So testing has, you know, has confirmed to myself and patients that, as well as the literature that this is really happening, that they're really maintaining and improving their telomeres.

And, you know, this is impressive. Yeah. I mean, when I have a conversation with patients, you know, sometimes they're there, you know, so they're sort of what's a telomere?

And, you know, you give them that great explanation of what it is for the molecular clock. And then they're saying, well, you know, why should I care about it?

And if you tell them about what they're dealing with, length is let's say it's average and okay. So then trying to slow down that rate is great. But some patients I've had have come in and they've had telomere length.

You know, they're in their 40s of like a 70 year old. And that changes their calculation. They're all of a sudden like oh. That's that's not good. And one of the reasons for that is partly lifestyle, but also, I mean, all the things we're going to talk about that can affect telomere length, but but also inheritance is a big factor of it.

There's about a 70% heritability of your telomere length. And so people don't know whether they have, you know, no pun intended, and sort of a little bit of a ticking or a ticking time bomb, because they started out with a kind of a

short reserve of telomeres.

Likewise, some people come in with really long ones. And, you know, I don't tell them to start smoking in that situation. Right. But, you know, I think that's why I try to encourage patients to get the measurement done.

But you're right. I mean, if they don't want to pay for it or not, but still doing whatever you can to, to improve telomere length or to keep it from getting shorter is, I think, a very, very important thing.

So one of the things that you kind of employ to help besides, direct telomerase activation to, to keep your people's telomeres healthy. Okay. So we know all this stay healthy business affects telomere length.

And, you know, you can start looking at any, direction and we'll kind of hit a few of them one by one exercise. Well we know okay. Every we if we all there's the there's the elliptical in the back I should be I should be on about.

Well we're talking, but, we know all the all the benefits of exercise. It's free. It's, you know, the health outcomes obviously are, you know, very, very impressive and part there's studies know that part of the mechanism of health improvement through exercise maybe you telling me related concepts in mouse studies.

Mouse where there took my, target minus minus so that, you know, the reverse transcriptase is, enzyme is missing. You put them on a little mouse treadmill, and they don't improve in VO2 max like the control mice.

So this might even be part of the process. So you guys that that have telomeres and various other studies, nutrition studies compare. There are studies evaluating how Mediterranean is your diet olive oil legumes etc. etc.

and the better. This is part of the nurses health study. Huge numbers. The more Mediterranean diet the better the telomeres. And in terms of environment, we know poverty is associated with for telomeres for all the reasons nutrition, proximity to pollution and traffic, the separate distance from freeways is is a factor.

So, you know, so unfortunately poverty is a factor in telomere loss. And, Important stress reduction techniques. Right. And independent studies of yoga practitioners versus non yoga practitioners controlling other variables that have telomeres.

Meditation. Each little component has been looked at separately and in fascinating studies. So to of all this is feeding together nutraceuticals. We're going to talk about we can throw in right now and there's a, there's a newer study combining.

They have a very advanced nutraceutical, mix including probiotics and omega threes. And, and all is like, this is the, Yeah. I was just looking at that. Go ahead.

Yeah. So color study. Anyway, each of the circles been looked at individually, especially the ones, you know, that we have tremendous data on and health outcomes, vitamin D and what doesn't it do better?

Telomeres or omega threes.

Measuring Telomeres and Lifestyle Factors

And having an adequate balance of all the antioxidants I think is important to first remember it's our struggle against oxidative stress. So, you know, telomerase helps.

But if you can come in from the side and reduce oxidative stress, remember that intelligent antioxidant idea? You can reduce oxidative stress with coenzyme Q10.

Okay. Your mitochondria are in better shape. They don't need as much of the telomerase. Then they can move over to the nucleus and protect the genome.

And so all these little things come together. Yeah. That's what I've always been fascinated by before I even knew anything about telomeres, which is probably prior to 2007.

Oh, I'm sure I heard about them before that. You know, it was fascinating to me that everything that we knew was good for your body helped to keep you on years longer, and everything that was bad for your body was associated with shortened telomeres.

And it kind of also, you know, it all really kind of made sense. And then remember, that test, which we still can do is the eight hydroxy two deoxy go is the urine test.

You know that was our test for oxidative stress. Well what is that. That's the GG person's getting you know, taken out of the DNA because they're damaged and showing up in your urine.

So, you know, when you see that kind of kind of stuff happening over and over again when you're reading and as time goes on in telomere biology, it's really pretty fascinating.

Yeah. That is together. Remember that the that's why, you know, the gap is this is why, you know, you know the telomeres so sensitive to oxidative stress.

Yeah. So it's great how that fits in. Yeah I always talk to patients about a seesaw. Basically it's as simple as the things that stress telomere length for, briskly proliferating cells, oxidative stress, you know, all the bad things, balanced by how much you can do to prevent those.

But and then telomerase activity essential and even even, you know, mental stress. Is there another quite a few reviews going through the connection between just, you know, stress and, perceived stress and how this all fits into there's a study that recently published on this.

So, you know, we got through. No one's going to no one's lifestyle is going to be perfect. But obviously you do what you can. Now, adding a telomerase activator like De 65 gives you, a step, a leap forward on this as well.

Yeah. You know, both my parents passed away from Alzheimer's disease, and there was a lot of stress, you know, around the family. And I always found that, you know, doing exercise took some of that stress off of me.

And I was very relieved to see that actually, exercise can mitigate the shortening of telomeres. It occurs with perceived stress. So, you know, it's it's all again borne out in the in the biology when you know what you're seeing in everyday life, which is which is really pretty fascinating.

You talk a little bit I mean, both you and I do hormone optimization talk a little bit about the role of hormones in telomere biology and telomerase activation.

Okay. Right. There's another dot that would connect oh, in terms of Alzheimer's, we know Alzheimer's. And and non Alzheimer's dementia associated with significantly shorter telomeres.

Recent study and mouse model of Parkinson's treating with to 65 improves their actual behavior in performance, balance and all types of things that, Parkinson's mice, mice can't do.

Well. So back to hormones. You know, the whole field of hormone optimization evolved from it was considered a great thing. And then do some for these studies, like women's health Initiative, which measured, you know, equine estrogen and, you know, artificial progesterone, which was the progesterone progestin.

And all of a sudden it was bad. But then, then the the wheel turned. And again, that bioidentical hormone optimization doesn't have increased cancer is a tremendous quality of life benefits.

So this is often a reason why people will show up in a preventive medicine or anti-aging, practice because of, hormone deficiencies. You know, testosterone in men or menopause and women.

So of course, we, you know, have ways of measuring and clinical evaluation and then replacing now I've before I again, before I even really had studied much cellular science, I was doing this and lo and behold, this a direct connection.

Just about every hormone and its telomere effect has been has been studied. Estrogen and progesterone in women, testosterone in men, growth hormone. When there's adult growth hormone deficiency in both men and women, melatonin that's another one of these.

What does it do. It kind of interventions all associated to, you know, optimizing the youth levels, not, you know, again, what we want to do is optimize human physiology.

We don't want to use doses that are outside physiological ranges. All this is another branch to improve telomeres, right? There's also you know, I was stressing that there's direct evidence that estradiol is a modest telomerase activator.

Five alpha sorry, DHT. Creation of DHT from testosterone through five alpha reductase is a mild telomerase activator. IGF one is a mild telomerase activator.

Maybe part of the reason why growth hormone, testosterone and hormone replacement therapy with estrogen and women. Part of the beneficial effect, is through telomerase activation.

And we'll talk about some of the other non-canonical activities of telomerase. The other fascinating thing is that we were talking about stress cortisol, telomerase inhibitor.

So the molecular mechanism for why stress can be detrimental to your health, further evidence that, you know, these things are all interrelated. Right?

So we don't need a mystical explanation of what you of why stress does this. We actually can have a biochemical thought, you know, scientific explanation.

And again, in testosterone, when you treat men with testosterone, you're really treating with three hormones because aromatase is the estradiol and five hours reductase to dihydrotestosterone.

So you're getting getting all three. Yeah. Which is again why I always try to tell the doctors that we, you know, educate that you have to be careful with these aromatase inhibitors, to try to keep the ascertain level down.

It's always thought that it's a bad hormone in the male. It's not. And you got to keep it a level. Not not but not to dilute when women need testosterone as well.

And also on that, on that subject, I, you know, not a fan of five alpha reductase inhibitors because of, again, you need DHT and associated, cognitive dysfunction, depression, erectile dysfunction.

So again, these hormones are part of our our natural hormone profile. Right. And some of that may be mediated through to, to, to to mere biology and telomerase activation.

So that's a fascinating thing. The telomere biology is right in the middle of it all. Yeah. It really is. So you were talking about, the sort of non-canonical, aspects of telomerase.

I remember when I first started thinking about tumor biology and what effect it might have in aging on a sort of like, well, you know, it's about cells dividing, but some of the most important cells in the body, you know, the neurons, the cardiomyocytes, the heart cells don't actually divide their post mitotic cells.

So how could telomerase be that important for aging? Well, of course we know what that what some of the mechanisms are I want to talk a little bit about that.

Yeah. So right. So first you know in terms of the post mitotic cells, you know, cardiac monocytes, neurons. Well, they're really not completely post mitotic because there are stem cells in the heart and in the brain.

And another one of the non-canonical effects of tert is to preserve stem cell function as a whole. This takes us in a whole other another direction. So we've got because we are somewhat repairing our cardiac myocytes and neurons.

So we know that, you know, can better cognitive function, less depression, all the neurological diseases associated with longer telomeres, even if they're not directly making the telomeres in the neurons longer versus supporting the glia in terms of the brain.

You know, I think those in medical school, I think it was the concept of glia something oh, it's like packing foam, right. It's like the peanuts. Yeah. It doesn't do it.

But then we know that the metabolism of the glia is essential to the neurons. So and they are mitotic. So preserving the telomeres and the glia. Plus again having the protection against oxidative stress for the neurons is big.

And even if you it's not a matter of adding more telomere sections protecting against inflammation. You know, fire in the brain is all the, all the cognitive dysfunction related to inflammation, protecting against inflammation, protecting against oxidative stress.

We'll protect these post high tech neurons, you know, cardiovascular that that telomere length. There's a lot of studies. There's one correlating with coronary artery calcium score.

That's better. Others just with major cardio of adverse cardiovascular events. So even again if the myocytes telomeres aren't getting longer, something good is happening to the cardiovascular system and the cellular function is preserved.

And that's another key thing in and cardiovascular system. So the endothelium, you know, needs to keep its telomeres like these. So you don't develop diastolic dysfunction.

And that whole cascade. So again post mitotic cells need telomerase from you know, from the components in the term.

Hormones, Stress, and Telomerase

And now there's some papers suggesting the RNA template. The turret even has non-canonical functions as well. So you in biology again opening one little window.

Now there's a whole new world right. Yeah. Well we had our the first cohort come through our practice that was taken to 65. We found significant effects on the immune system and remodeling of it, which we'll talk a little bit more about.

But, you know, a second paper that we published, a couple of years after the 2011 paper, we talked about, the metabolic things that happen, the improvement in cholesterol and blood pressure.

And, and, you know, it was difficult to know whether that was real or not because it wasn't a randomized controlled trial, and they were taking supplement packs that had potential beneficial effects.

But then, subsequently, Fernandez at the University of Connecticut did a study looking at, 65, in metabolic syndrome. And they found similar results in a crossover controlled trial.

And one of the reasons for that is this link between the telomeres, and telomerase and, the sort of master regulators of the genome, p53 and PGC one alpha and beta.

So, you know, even if the cells not the binding, you get that improvement in mitochondrial function and mitochondrial biogenesis. Yeah. I mean, you need this p53 balance, you know, because, too much can be destructive.

And to literally take me you lose protection and in terms of, you know, my clinical practice, you know, I think and, you know, the first thing you might say, oh, anecdotal but experienced, this is how experienced clinicians learned through the years.

And, maybe we'll talk a little bit about this later. But one of the comments and the observations on 65 is without seeming without really other variables changing that.

Hypertension improves. And so typically a patient will say, well, after starting 65, you know, like I cut my whatever, you know, I'm low to being in half.

And then two years later I kind of forgot about it and my blood pressure is okay. And again, everything we're doing should help. And, you know, weight control obviously and stress reduction.

But when it seems even when that's the only thing not all the time but it's, it's it's a change that I've been observing time and time again. Yeah I as well I mean, I have as you I'm sure do as well have some relatively elite master masters athletes in my practice.

And, you know, these are people that follow their metrics quite closely and they'll see things like improvements in, in their times or recovery time, for, you know, for their whatever distance they're running, or cycling or swimming, and that, you know, could well be because, they are increasing their mitochondrial biogenesis, the efficiency of their mitochondria or perhaps is, you know, less the, a fewer inflammatory cytokines because of the mechanisms that have been worked out with, with, with, with, with, you know, making sure cells don't become senescent.

Right? Like, oh, yeah. Didn't mention, you know, the senescence one of the so the the acronyms and CSP senescence cells, you hear a really secretory phenotype.

So you say when when you lose tell them telomeres you got a few a few bad things can happen. But cell you can just have senescence with the cells over replace dead.

Worse yet you can have the cell become a little inflammation factory producing this CSP. And that's the concept of the bad apple. So the inflammation that this cell that's lost its telomeres producing is affecting all the cells in the neighborhood.

And then getting things even worse now you can have genome instability, breakage fusion bridge of, you know, of of the DNA. And this can lead to mutations that can, become malignant.

So, the use of this is this, that when you lose telomeres, the cells become inflammation factories or SARS, the generators. And this affects the entire body because we know like, what's the the biggest lab test risk factor for cardiovascular events more than LDL cholesterol and C-reactive protein.

You know, it's your overall inflammation score, right in that to the two markers that are part of the senescence associated secretory phenotype. Or as you mentioned, pi, L6, TNF alpha are the cytokines that increase C-reactive protein.

C-reactive protein, then is the one that, you know from the Ridker studies and, a couple of decades ago, showing its association and through to the Jupiter trial, where, you know, people with normal cholesterol, if they had a high C-reactive protein, protein, and you brought it down with the statin, you would see improvement in events.

That's where the inflammation is important. I think that's, you know, important, thing, thing to understand. You know, I think I often tell patients, and when I lecture, I talk to them about fuel.

Your life is as good a predictor and independent of other traditional risk factors as, hypertension, cholesterol, and, diabetes for cardiovascular disease risk in, in large prospective, you know, association studies.

But, but, you know, I, you know, you often have patients come in, you know, I do a coronary calcium score and all my patients, you know, have risk factors.

What's going on here? Still have a family history, you know, have a high cholesterol. Their blood pressure is okay. I got super short telomeres that that's that's part of it.

And, you know, if you're aware of the the studies going on the tactic trial in, and okay. Right. Yep. That's that's the same sort of theory. Right. So that study, you know, under underway not not results, not published yet, but looking at the relationship between inflammation we telomeres inflammation cardiovascular events and.

Right. So this in this way. Yeah. I mean can spread this it may be through anything else cell regeneration. But I think since it's looking at person within MI within six months and geographically demonstrated, and then see whether or not the year of 65 keeps them from having a recurrent MI.

But mostly what they're looking at is the, whether it reduces senescence T cells in it, because it's the senescent cells that are setting up that inflammatory milieu, which then changes the T regulatory cells, which they say is so important.

And, you know, for those, those actual events, that that's their primary endpoint is a reduction in senescent cells. And, you know, that's sort of what we showed in that original trial in, the cohort in 2011.

We showed that reduction in senescent cells fascinating how it figures into cardiovascular disease as well. Yeah. Well, that's what I've learned from you, how, you've got your naive, healthy and senescent and, you know, the CD8 positive, 28 negative.

Once you there, you know, the senescent cells that not only don't work, but to quote to quote, you know, they they crowd out the immune space. That's right.

There's no room. There's no room for the, young upstarts who want to fight, you know, inflammation and infectious disease. Right? And not only are they not, Not only are they not doing their job correctly.

Oh, I got lost my picture here for a second. Okay, but they're like the they're like the, the old watchdog and barking at the neighbors and biting their owners.

You know, they don't they don't get the bad guys because they can't see them. But the people that are nearby, which is, you know, one of the major factors that happens with senescent cells, they adversely affect their neighbors real nearby through these paragon, activities and cytokines that you get, you get adverse effects that way.

So, yeah, I mean, I think that we think about cardiovascular disease now, I think more as a, as an inflammatory disorder than anything else. And so the immune system is so critically involved.

Yeah. So this all fits together with, you know, the concept of G. It's not just the LDL. It's got to be oxidized. What turns on the oxidation of LDL, it's inflammation.

And then what turns on the adhesion molecules that grab the monocytes into the end of the ilium that became item. And, you know, it all fits together.

There's hormone branches on that to have hormones going to inhibit it. But again, if you keep digging deeper, seems like the telomeres telomerase are in the center of the target.

Yeah I mean I think they're they're sort of the, the, the upstream kind of regular regulator of everything. You know,

we also just published in, in April online.

It's not yet even in PubMed as far as I can check real recently. But, there was also the randomized control trial showing, you know, I've talked about it.

You've heard me talk about the Spiess trial before, in which we looked at whether 265 could lower senescent cells, as defined by liking CC 28 positive 28 megs.

And in fact, we did see a about a 20% highly statistically significant reduction in them in a 500 patient trial. So, you know, it doesn't. And I see it in my practice.

I measure the senescent cells, and I see reductions. I've seen reductions up to 50% at times. And in the I've seen the published version, but in the preliminary version of, of of your paper there, I never saw a p value with so many zeros before the one that's how do you what do you remember about that.

But talk about significant. Yeah. It was, it was it was really gratifying to see you know that's that's that's the fun thing about what you and I do. We kind of sort of said we get to see in our practices the effect of cutting edge science, on our patients in beneficial ways.

And then, you know, also, you'll see it played out in randomized controlled trials as well.

Non-Canonical Telomerase Effects and Disease

You know, you're practicing good objective sort of what do you what do you call yourself now? Longevity medicine, anti-aging medicine. Age management medicine. It's a field looking for a name.

Some people don't like the antique pot, even though the biotics prevent it's preventive medicine. I don't know how to know about that. It's for it. And that's it's kind of overlaps with primary care because you can't separate them completely very well.

Yeah. But the same thing, you know, in terms of the, you know, senescent cells, of course, in terms of viral infections, go with, CMV virus. But, there's even some papers in the past year since the, during the pandemic, you know, discussing the Covid 19 relationship to, Cd28, CD8 positive 28 negative cells and suggests suggesting that so that the 65 could be an into an intervention.

And, the shorter the telomeres the the greater the mortality from Covid 19. Right. I don't think the comorbidity factors cardiovascular disease, diabetes, well, these are short telomere diseases.

Age is obviously a big comorbidity. That's a that's that's that's the issue of telomere things. So it really does fit together. And of course we it would be difficult to really study this and come to a specific conclusions.

But logically it's got to help. This would apply to all kind of like rapidly, multiplying viral illnesses, all these rival Ebola virus, even HIV, you know, burning through your T cells, you're going to end up with senescent ones.

And that is our chance to, you know, rehabilitate some of them to actually work for us. Yeah. I mean, speaking of sort of, sort of regenerating things.

And, I was speaking at a conference this past weekend to regenerate physicians about, you know, potentially why they should think about telomere biology in their work, any kind of stress, be it the stress of a joint that's undergoing, you know, too many marathons or or too many, you know, too many cycles, on a bicycle, any kind of stress for the surf.

Right. Exactly. For me, we'll be getting back up on the board after falling off too many times. Any kind of stress requires your system to then, you know, breaks down cells, then requires them to to to divide.

And what we're finding is that the these chronic viral stressors, particularly in the herpesvirus family, you know, you mentioned CMV, we didn't we didn't talk about that in death, but that's herpesvirus number five that most of us did when we when we were first training.

We're sort of like it's benign. Don't worry about it. Then we live to the, the Aids, the, you know, resurgence, epidemic. And then we saw that people were dying of CMV when their immune systems weren't working well.

So your immune system has to work well to keep it at bay. But if you if you do have, you know, sort of a subclinical infection, you're seropositive for it.

It makes your immune system work harder to keep it. And it makes you have an increase in senescent cells and shorter, shorter telomeres. And so when Covid came out, I saw those hypotheses papers that you're talking about, where they, you know, the research of the leading researchers in the field were saying, you know, why did this 40 year old, healthy, seemingly healthy guy succumb to Covid?

Well, you know, did he have CMV? Did he have a high accumulation of senescent cells that were more like a 70 year old and therefore biologically, he was really like a seven year old?

This is kind of stuff that it's easy to have. Sera. They should look at it. I think they probably are going to start to look at it because, as you mentioned, they did published papers.

Maria Blasco and and I think a French group published papers about if you had shorter telomeres, you had more severe Covid and higher mortality because you just don't have the reserve.

A term I like to use is a biological 401 K. You know, you got to keep that. Yeah. Keep that up. So that you can keep on and I guess. Yeah. Just yeah, just like a 401 K where the employer and the employee can contribute, your lifestyle can contribute, and the 65 can contribute.

Right? Right. There's some other stressor. Any other, strategies that you use to, sort of educate people or to, to monitor them on it. And then, I think we talked about protecting post mitotic cells.

Yeah. Anything else that, that, that you wanted to light environmental toxicity. You said, you know, fortunately, a luxury of this type of medical practice for me is I have time to really sit down and talk to the patients and get and I really get to know them.

I mean, some have been with me now 23 years. I mean, I know them and they, they they know me and it's, it's, you know, it's, you know, this is the you know, this is the way medicine ideally can be, can be practiced.

So part of it is, you know, explaining, you know, what we're doing and why in terms of everything in terms of hormones, in terms, you know, certainly in explaining the whole telomere, telomerase, picture and from the lifestyle.

So you see the Da 65 and, you know, there's a lot of products or supplements that claim to be telomerase activators. And but claim is the word as far as I, you know, as far as I know, the only only nutraceutical that has published data on this is the 65.

And so a lot of things well, who knows, it might work, you know, might be in the category, might help. Probably doesn't hurt. Who knows. But if you why pick something from that category when you actually have literature that documents the effect of this?

So we go through it and, and you know, again trying to talk to patients and let's, let's work on that program. Sometimes people will come in with a shopping bag full of supplements and dump them out on the table and say, you know, this is what I'm taking.

And of course, very often they're redundant or who knows what. And I said, well, let's try to prioritize things in terms of, you know, benefit and what we know about it.

And, let's go through your list and some of those people also, in terms of supplements, there's a burnout factor. So yeah, okay, I, I I'll take 5 or 10 or this or that.

Okay. Let's for you in your particular situation what's decide what's most important. And then we can discuss you know how things fit together. And I can explain why I think, you know, 65 is so important.

And of course the question is in this kind of practice as well, do you take it and, you know, the old bottle of medicine. Oh no, we're loose. You know, you can't, you know, but no. Yeah.

Because hey, if it's so great and you don't take it, there's a disconnect. But and you know, I explain. Yeah, I do. I've been doing it for, I don't know, five, 4 or 5 years, now.

And I've had, you know, 3 or 4, life length tests along the way, you know, some some jump, some steady, some a little zig zag, but going up. So spending time to go through, what are they doing, where do they.

And you know this whole everything course cost money is not unlimited. And how do you want to invest your money and your health and healing? Having a discussion like this and explaining the importance people will, you know, which I'm trying to convince them to do what I think will keep them the healthiest.

And so I probably have, I don't know, 5060. So maybe 80 patients, they regularly have been taking their 65. Yeah. And sometimes they ask, you know, it's a it's a supplement.

It's a little bit expensive. What do you tell them when they ask you it. Was it safe to take have there been, safety, studies done on it? You know, you know, we we know that that it works to turn on telomerase because of the trap assay, which is the gold standard.

But, you know, has there been, you know, animal studies, etc. and, you know, I tell them about the fact that it started out sort of as a drug, even though it's an extract of the traditional Chinese medicine.

And, but, you know, it went through the initial safety, experiments to, to make sure that it, it was safe. And now it's generally recognized as safe. And, what what kind of conversation do you have with them about this?

So it has this generally great, generally recognized safe status. I mean, that means you can make it a medical food. You get it. Right. You 65, protein bars, something like that.

So that and there's really no reported adverse events linked directly, you know, to, to, to a C, a 65 and, let's see. So again, you know, we're only the only one thing we're all losing telomeres except of the for immortal animals.

Right. And that, you know, we talk about that and I know it sounds funny. What immortal animals as well, you know, like a sea anemone. Well, it's not immortal.

You know, you could step on it or eat it, but it's immortal in the sense that it's germ cells and somatic cells well mixed together. So it reproduces by budding.

So theoretically, the first CNN and the ever alive is still alive. And how do they pull this off? They have a lot of telomerase. And then we talked about even sometimes, the giant leatherback, leatherback sea turtles that live pretty much indefinitely full of 500 years.

And, again, they're they produce a lot of, so telomerase to keep going. Then people sometimes ask them, well, how do they die? And tragically, they'll eat plastic bags in the ocean thinking they're jellyfish.

So we would learn a little bit about the biology of other animals and telomerase too. Yeah. And I also I talked to patients about the, the, cases of, telomerase.

And these were people, you know, in humans. So people are like, well, what's a turtle? You know, what's a shark?

You know, I'm talking about me as a human, right?

But if you have just a 50% knockout of telomerase activity, not the whole thing, but just 50%, you are going to have a shorter life.

Clinical Experience, Safety, and Outcomes

I mean, these people, they if they have, you know, severe ones, born with the short, real short term years, if they're second or third or fourth generation, then they die in their 20s.

If it's your first mutation to have 50%, then they'll die of pulmonary fibrosis in their 50s. But a lot of them are dying of bone marrow. The tissues that need, more high turnover.

So telomerase absolutely is important for longevity. We see that. And then the other thing that patients often ask is, you know, you're quick, you're quick, discussion with them about, well, all cancer the 90% of cancer cells have telomerase active in it.

Is this going to increase my risk of cancer? Right. This and this is an important part of the discussion. So the concept is that for cells to become malignant, there's a whole series of mutations that have to happen.

Having to do with retinal, retinoblastoma protein and many other things. But for a cell to be malignant, it needs along the way to express telomerase, because if it had an Ace like limit and again rolled over and played dead after X amount of replications wouldn't be a problem. Metastasis wouldn't be problem.

So one of the mutations that along the way has to be to express telomerase. Also loss of contact inhibition. For another example, cells like the clump together with their time.

And so to become metastatic they've got to go platinum floating off. And so the question is well gee could a telomerase activator boost cancer somehow.

But you can. First the big cancer malignant cells already have it right now. Maybe there could be some fine balance in shutting off telomerase to get rid of the living cells and and turning on again to protect the rest of the cells.

This is, you know, something to be determined. And certainly in all the animal studies about, you know, mice that a couple of years they usually die of some kind of cancer.

You know, other, you know, renal disease, but no, no increase in cancer risks. And there's no observed increase in cancer as in humans. In fact, just about all cancers are associated with short telomeres.

That's right. So on and on and on. And you can see why shorter telomeres genomes not protected. All it takes is that one malignant mutation could have been years ago.

And for that but that cell line to start multiplying. So we got very strong evidence that short telomeres are a cancer risk factor that cancer already has it.

So turning on telomerase in other cells to protect them isn't going to give cancer a boost. Yeah, that's a key, thing that I tell patients are sort of like, you know, cancer cells have turned on what we call constitutively and, and, and, so if you turn on telomerase modestly and transiently, which is what a molecule like to 65 does, it's like a drop in the bucket.

Whereas the long term studies we have brunet Italy and then the biggest one from Copenhagen where they looked at thousands and thousands of patients from the bottom 10th percentile to the top 10th percentile.

You have, that is longest, longest being the top ten percentile, shortest being the bottom ten percentile. You have about a one and a half fold increased risk of both cancer and cardiovascular disease.

That's the important data in real life. Short telomeres increase your risk. And then remember, in studies done by, Harley and all in fibroblasts, you turn it on even constitutively.

You're right. It needs other mutations. He cells are immortal, but if they don't have the other mutations, they don't they don't turn into cancer cells.

So I mean, that's why I mean, that's why I've been taking the 65 for 14 years now and treating hundreds of patients like you with it. And, and when watching the beneficial effects, of it over time.

So, yeah, I mean, look, I think the I'm looking forward to the results of, the tactic trial and then, you know, more papers coming out on, you know, the role of telomere biology.

Do you have any closing thoughts about what, what you think, the future is for you in the practice and in particular, just getting feedback clinically, like I said, that an email to my patients taking VA 65, no suggestion.

Any observations and the kind of more consistent comments. Well, first, there's, esthetic things, skin, you know, we, you know, our practice is anti-aging, but from the inside out, we're not involved in late laser treatments, etc..

I mean, I believe that for some of the others with their expertise. So comments like, well, gee, I didn't see so and so in so many years. And they just said, well, what did you do?

What did you do to your face? Is it you know why he looks you look younger. Okay. Interesting. Other come another comment again not in everyone but occasionally are visual changes.

Now we know this that does study improving you know, a macular degeneration. And so and the theory is that, retinal epithelium is improved, but presbyopia I have two patients, both physicians who comment was I don't need my Close-Up glasses anymore.

And when I've mentioned this in various lectures and seminars, a couple of hands go up to me to see you speaking about homology study downstairs in the buildings, as well in your community. 65.

No, impossible. Well, what do you think it is? I don't know, okay. And it's not a very productive this guy said I've had this is bring pre and post eye exam numbers and yeah looked it up and some of it what is effective like quote I don't need my you know my like many close up glasses energy level and that's that's pretty nonspecific and so many things feed into it.

But that's a very frequent comment. The more energy. And some people interestingly, some people take it as if I played and I'd say it improves sleep. Some my patients said they take it late, it's harder to sleep.

They're kind of wired and they take it in the morning. So something's going on. Comments like peripheral neuropathy improve improving. Yeah. And a few patients not non-diabetic peripheral neuropathy.

Attention deficit disorder got common was, you know, this is what I need to focus better. And, one interesting is, let's I used to have to take 20mg of, to Delafield, but now five works.

And this is the athletes change. Okay? That's saving a lot of money. You 65 right here. And so, you know, all these interesting comments and people vote, especially in a product that's not inexpensive.

People you know, people you know, they're voting with their wallets. And I'd say almost all the patients who've studied under 65 have continued. And so that's I mean, that's an interesting observation, but, yeah.

No, I can second that in my practice as well. They typically, they do continue in that particular opacity too. Oh, that's interesting. In my personal case, just as a, as a surfer, when there's bigger waves here in the winter, you know, I get held down on the water just coming up gasping with a little oxygen that would, that would help.

And I notice that again without anything else obvious that when I started to 65, six months later, maybe I was just getting through the bigger surf, better I wasn't I was kind of didn't feel as oxygen deprived.

I didn't really measure my as Max. But comments like that in a lot of athletes. So actually, who do you write? Some of the athletes have one. Well the numbers and they commented the VO2 max has improved.

So there's all these clinic, you know, clinical benefits that you can see in patients. So as a clinician you want that to the theory. You want the published papers and you want to see what's going on in your patients.

And then you put it all together. Yeah. You're trying to keep people happy and healthy. Yeah. That's that's if that's, you know, you and I, but I think it's been doing it's just about the same amount of time. And seeing that I haven't seen anybody necessarily stop because of adverse effects, and, and I've seen patients stick with it for the beneficial effects you're talking about.

And also, you know, maintaining telomere length, I, I measured telomere length in all my patients, you know, at least once a year and watch them and have, you know, over the last 14 years if you haven't lost any telomere length, that's key because the critical thing is relative telomere length.

If yours are shorter for you, then gene expression changes and all sorts of things change. Mitochondrial function changes. So if you can keep it at the level that it is, then, you know, you're pretty much doing a really great job of slowing down the aging process in a patient.

Yeah. And that's been my observation as well. That again, there's, you know, varies from patient to patient and there's some zig zagging. But in general people have either maintained their own or increased slightly or a few increased dramatically.

Yeah, I would say about measurements, is that I've had people come up to me and say, well, look, I took out a patient at 65 and did a baseline measurement.

Then six months later they're up. You know, point 2 or 3 kilo bases, which, you know, tell me is around eight kilo bases in young adulthood and then around a six year old, maybe around six kilo bases if I feel a five and a half kilo basis.

So point to, well, I'm sure this is a significant it's a I was about 4 or 5 years of aging, but there is that variation in the measurement. So one measurement, six months later it could have been down 0.2.

It could be half point one. It's not going to be a 0.5. But I think, you know, particularly in people are saying, you know, it's gone down. And so I shouldn't, you know, it's not working for me.

You need about 2 or 3 and 3 or 4 measurements over the course of a year or two to really know what the trajectory of the, of your tumor like is, because there is that up and down.

It's been called a pseudo telomere lengthening and shortening, because it's really about the, the characteristics of the, sort of relative, fractions of the cells.

The white blood cells are floating around. For instance, if you exercise vigorously in the morning, it mobilizes senescent cells into your blood. They have shorter telomere length.

Therefore, if you did their telomere length measurement a few hours after that, you're going to get slightly shorter telomere length than you do the next day with actual no actual change until really just the population.

So you got to watch out for that. If you're if you're, if you're measuring telomere length and just sort of say, you know, you're not a day trader in it, you're you're in it for the long run.

So we should do just that. Everything in medicine lives, as we always put in perspective and not be obsessed with

the exact number. And look at the big picture.

Well, Ron, it's been great talking to you. I think we've been talking about about an hour now. And, do you have any final thoughts on it? Okay. Well, I'm very fortunate personally to be in this field, and it's allowed me to can, you know, continue, you know, be happy being happy.

Happy and healthy. And a big part of it is that 65, along with everything else. And, I think the work you're doing in this field is really great. And, I really appreciate how you you, you know, advancing the field and bringing this information to everyone.

And thank you very much for, chatting with me on this. Well, thank you. It's been great talking to you, as always. And, you know, you don't look any different every time I see you the last number of years.

Keep on surfing, keep on keeping people healthy. And, I'm sure I'll see you shortly at the next conference. Okay, I hope so. Thanks a lot. Take care. Right.