Introduction to PCOS and Brain Health

Welcome to this episode of the PCOS SOS Summit. I'm your host, Dr. Felice Gersh. With me for this very special episode is a famous, renowned, incredible neurologist and Alzheimer's researcher, Dr. Dale Bredesen And we are going to discuss some really critically important information that most women with PCOS know absolutely nothing about their brain health.

This is not a little deal. So welcome, Dale. Thank you so much for joining me. This is so incredible that I get to interview you and first, before we delve into this really important topic, could you tell our audience something about you and your research and how you got involved in this incredible issue of Alzheimer's disease in terms of its evolution and its therapeutic potentials?

Thanks so much, Felice. Great to be with you. So I spent my career we worked for 30 years in the laboratory looking at one fundamental question, which is what is the basic molecular driver or drivers of neurodegeneration?

Why do you get Alzheimer's or Parkinson's or Lewy body disease or, you know, on and on, so many different things, frontotemporal dementia, ALS. So we spent a lot of time and published over 230 papers on this looking at what actually drives this.

And I have to say, the big surprise, we finally began to translate all this research back in 2012. And I saw the very first patient I hadn't seen patients in over 20 years.

I've been working on mice and fruit flies and cells for all that time. But we saw the first patient in 2012, and I was actually so pleasantly surprised that she did extremely well, improved her cognition, and called me after about three months at my home on a weekend to tell me how great she was doing.

So I was very enthusiastic to hear about that. And then we began getting Case after case. We've now had over 7000 people who've been on our protocol. We published a clinical trial last year, which is a proof of concept trial.

It's freely available online, as our other studies are. And this came out in the Journal of Alzheimer's Disease. So you can take a look at that any time.

And and in that in that study, 84% of the people actually got better. Didn't just slow their decline. They actually got better.

Dr. Bredesen's Research and Alzheimer's Reversal

We have people now who have been better for over ten years. As I mentioned, the woman who got better in 2012 is still better. And she's now 11 years into this when normally she would have been either in a nursing home or passed away.

So we're very enthusiastic that the research translated very well into what you can actually do to prevent and reverse cognitive decline. So I would argue that now if everybody does the right thing, we can make Alzheimer's optional.

What a wonderful thought to think that this massive killer, I mean, it's one of the main drivers of death of people. And, you know, it's just what it does to the family members is unbelievable.

I see so many of my patients who spend several years caring for one of their beloved parents who is in decline with Alzheimer's and it takes down the caregiver as well as the one they're caring for.

It's such a huge, unfortunate epidemic. They're talking about it growing by leaps and bounds. And here you're saying it's preventable. And that's really what I love to focus on is prevention.

But I love that you have not just prevention, you're actually reversing and which most people think is impossible. So you've done what is generally viewed as impossible.

So now I want to add to your incredible list of accomplishments by helping to explain to our audience of women with PCOS. First of all, help them to understand and I will with you that they have many of the risk factors that underlie the evolution of developing Alzheimer's and what those are in general.

And then we'll bring it back to PCOS. And then, of course, we're going to talk about what can be done to help prevent this horrible, horrible condition.

And for anyone out there who doesn't know this, women have and you know the data I'm sure better than me. Something like two and a half times the incidence of Alzheimer's compared to men. And that's like age matched.

And so women are especially vulnerable to this condition. And I'll give you my $0.02 on why I think that is. But I'd love to hear what you have to say about what are the underlying risk factors that tend to exacerbate the occurrence of of Alzheimer's.

And then we'll see how that matches with some of the symptoms and conditions metabolically and reproductively that are, you know, unfortunately having to be dealt with by women with PCOS.

Yeah. And, you know, to put it in perspective, over a million people now have died in the U. S. from COVID 19 and about 45 million of the currently living Americans will die of Alzheimer's disease if we don't do something about it, which is why prevention and earliest treatment are the ways of the future.

And as you indicated, about 65% of the patients are women and 60% of the caregivers are women. So as Maria Shriver has pointed out over the years, this is unfortunately a woman centric disease.

So there and fortunately, there is a lot you can do. But let's go back for one moment to what the laboratory results showed us, because they really pointed us in the right direction here and what they showed when we studied cellular signaling, what is actually going on in your brain.

They showed that there are two major things that contribute to this loss of synapses, the loss of connections in your brain, which is what Alzheimer's is all about.

And one of them is energetics, the things that support your brain. And if you think about it, that's not too surprising. This is a degenerative disease.

You prevent it and reverse it by improving the energetics. And those are mainly cerebral blood flow. So you're looking at the blood that's coming into your head oxygenation.

So you want to make sure you're not dropping that, especially someone with sleep apnea is at risk, for example. The third thing is mitochondrial function.

So you want to make sure that your mitochondria, your batteries of your cell are doing well. And then the fourth is metabolic flexibility, the ability to go back and forth between ketosis and glucose utilization.

And in fact, you know, Felice, if you simply do a PET scan on a patient with Alzheimer's or pre Alzheimer's, the signature of Alzheimer's is reduced glucose utilization in the temporal and parietal regions.

So it fits perfectly with what we discovered in the lab. It's showing you you're simply not using this appropriately. And this is largely because of insulin resistance.

So energetics, one big one and the other big one is inflammation. So it's specifically your innate immune system activation, which is chronic and especially the memory part.

Core Drivers of Alzheimer's: Energetics and Inflammation

It used to be thought that the innate immune system, which is the older evolution free part of your immune system, the one that is associated with inflammation, less specificity, used to be thought that there was no memory, but it turns out that's wrong.

And in fact, the memory for the innate system lives in three sites. It lives in your bone marrow, it lives in your endothelial cells, which is why, unfortunately, people who have this high get these increased thrombotic and embolic events.

And then third, it lives in your tissue macrophages. So in your brain, those are called micro glia. And they're cells that will grab things like various pathogens, toxins and even things like amyloid.

So those are the two big things. It's too little energetics, too much inflammation. It's literally a supply and demand. Therefore, there is a tremendous amount you can do, starting with looking to see what's actually a risk factor for you.

Do you have insulin sensitivity? Do you have metabolic syndrome? Do you have obesity and inflammation? Do you have nutrient deficiencies? Do you have hormonal changes?

Unfortunately, all of these things are risk factors and I'm always after people also. Please check your oxygenation at night. It's easy to do. Wearables are being so helpful to us that you can check things like that in your heart rate variability.

Looking at your stress levels and things like that, we can address all of these things that are risk factors for Alzheimer's disease and as I say, literally make it optional now.

Well, when you say that list of all those things, it just rings so many bells in my mind concerning women with PCOS. So if we look at them, this is not talked about like the risk of Alzheimer's dementia for women with PCOS, it's hardly a peep out there in any of the literature.

So if you think about it and then we'll look at all of these things. So one thing that is very pervasive in women with PCOS is this low grade chronic inflammation.

Another is insulin resistance by age 40, A women with PCOS have about a seven fold increased incidence of diabetes compared to the regular population.

No hypertension, endothelial dysfunction like we talked about the artery lining and women, you know, one of the things that we can touch on is the production of nitric oxide, this amazing gas that helps to maintain the health of the lining and also prevent platelets from clumping and causing abnormal clotting.

And in order to have healthy arteries, you need the nitric oxide. And women with PCOS make less of it. So they tend to have more endothelial dysfunction, which of course manifests very heavily in pregnancy related complications, of course, which we now know is like the ultimate stress test of women and then sleep apnea.

You've mentioned women with PCOS have twice the incidence of obstructive sleep apnea and sleep disordered breathing. 80% have obesity and have abnormal dysbiosis and have leaky gut and have.

What's interesting is that they have a lower threshold to trigger the inflammatory release of cytokines compared to others, people's immune cells and also hormonal imbalances.

So women with PCOS, a lot of people focus only on the elevated androgens, particularly tests that's drone, but they

also have a defect within their ovaries with that process of converting testosterone into estradiol.

So they actually produce estradiol insufficiently. And one of the things that I would love to have you touch on as well is one of the things that endeared me to you instantly when I learned about your protocol for reversing Alzheimer's that for the women you always included estradiol.

So if we try to dissect some of these one by one and like talk about like what is going on in the brain regarding estradiol, regarding glucose like transport system, and then what about inflammation like what's happening in the brain.

So like, cause I love that you started explaining what's going on in the brain, so maybe a little bit more on that and then we'll talk about, well, going forward, like, what are we going to do?

Yeah, and there's a tremendous amount that everyone can do. So I think that's the really good news. This wasn't known 20 years ago or 15 years ago. We reported the first reversals of Cognitive Decline, published that in 2014.

More In 2016, 100 documented cases in 2018. And then, as I mentioned, a trial last year and we've just started a trial at six sites this year, which is a randomized controlled trial.

So there it's so clear that there's a lot you can do. But let's go back to the basics, because you can explain exactly why this happens. So if you look at the brain of someone with Alzheimer's, the first thing you see is that it is shrunken.

Unfortunately, it truly is a degenerative process if you are synapses. And the second thing is that you see these clumps of what's called amyloid. And amyloid is made largely from a single peptide, which is called amyloid beta peptide.

And so unfortunately, people have gone after, oh, that's that must be the bad actor. Let's just remove that stuff, let's suck that out of the brain. And that really has not worked very well at all.

So therefore, we want to know why is that there? What happens? And it's actually quite a beautiful story. So the amyloid is a little piece of a larger protein, which is called amyloid precursor protein or AP.

This AP sits across the membrane. So as part of its outside, most of its outside, a little bits inside. So it communicates the outside of the cell with the inside of the cell.

It is in many cell types, but mostly in neurons in the brain and mostly at synapses. So it's a perfect contender for things that are related to synaptic loss.

Now, what that does turned out to be fascinating. This thing is a molecular switch. So what happens is it goes back and forth when things are good, you've got not too much inflammation, you've got plenty of support, etc.

Then this thing is cut at a single site and it produces one peptide for outside the cell and one for inside, and it says Things are good. We're going to make and maintain connections.

And by the way, estradiol has a dramatic positive effect on that. So estradiol, as you know, binds to receptors in the cell, enters the nucleus, alters hundreds of genes.

And guess what? One of the ones that it increases is the one that cuts that AP at that single site, which is called the Alpha Secretase. So you can literally trace the molecular pathway of estradiol to make your brain function better.

Now what happens that same thing which is putting you in this growth and sustaining mode also when things are bad, too much inflammation, not enough blood flow, sleep apnea, as you mentioned, all of these problems come up.

Then it says, oh, I have to go into a protective downsizing mode. And by the way, this is the same thing that happened to our country during the pandemic.

What happened was early in 2020, we were told there is a new insult. SARS-CoV-2. So you're going to have to socially distance and you're going to have to isolate and you're going to have to not go to work, all these things.

And of course, the country went into a recession. This is the same thing that happens to your brain when things are not good. It throws you into a protective mode and says, Aha, you can't make those two things cannot grow right now.

Got to recede. And so what happens is you now get caught at three different places and you make four different peptides to four inside the cell to four outside the cell. And guess what?

NF Kappa B, which is one of the inflammatory mediators, again affects hundreds of genes, and two of them are the ones that cut at the beginning and the end of the amyloid peptide.

So you now have these four different peptides which are called Zap Beta Abeyta, the thing that everyone vilifies in Alzheimer's, JC Aspen, C-31 and these things are saying just the opposite change.

Put your resources not into new bridges, new synapses, etc. put your resources into protection. And by the way, the amyloid, again, that's been vilified is a wonderful anti-microbial.

So it actually kills viruses, it kills bacteria, it kills spirit kids, it kills fungi. This was first shown at Harvard by Professor Robert Moyer and Rudy Tanzi.

PCOS Risk Factors That Overlap with Dementia

And I think it fits perfectly with what we found in the lab. This is now switching. You're going into a different mode. Therefore, you're going to continue that downsize until someone figures out why it's happening and addresses those things.

Now, important piece, Ruth, respect to the inflammation part. Well, what kills us when we have we have COVID 19, it is cytokine storm, as you know, this just dramatic outpouring of cytokines.

And again, there it's because the innate system and the adaptive system are not aligned. Normally what happens is the innate system turns on the adaptive system which seeks out the pathogen, destroys it, everything's cleared and it resets the innate system, and now everyone's happy and you're now not inflamed again.

But with COVID 19, you just don't get there in some people. So you die of cytokine storm. Well, guess what? In Alzheimer's, the same thing happens. You've got an ongoing problem.

You're not able to clear it, but it's not as dramatic. So you're dying of cytokine drizzle. So instead of cytokine storm, you don't die in a week, you die in 20 years or 25 years.

And in fact, that's been one of the surprises I was taught that this is a disease of old age, 6070s, eighties, nineties. Guess what? It turns out very well documented the underlying changes in your brain begin 20 years before a diagnosis.

So this is really a disease of our thirties and forties and fifties that is being diagnosed far later, which is why, again, if we jump in early, there is so much that can be done.

So that's how estradiol is so critical here because it's pushing you over. It's one of the features that pushes you toward the growth and maintenance side and away from the protective downsides.

Now, of course, if you still got ongoing inflammation and you've still got ongoing pathogens, ongoing toxins, you

can't move it back there. But once you address those things, all of these things together literally change this molecular switch so that you are again in the growth and maintenance mode.

Wow. I mean, this is so amazing. I hope all of you heard, you know, that all of that focus was a little bit misunderstood, you know, on the amyloid data.

I mean, we just have to let it go, you know, and move and understand what it does and what it doesn't do and then focus on these new understandings which are so huge and including the benefits of my favorite hormone estradiol and what it can do in the brain.

And of course, on the opposite side, you know, what happens, like you said, if you don't have that and then what happens to the brain? It goes into this other modality stage, you know, that is theoretically protective but not, you know, not when it just never ends.

So if we look at some of the other issues like, say, insulin resistance, like what is the the biggest role there? I know some people say, oh, that's okay, just eat fact, you know, like, is that an okay substitute for not having proper glucose transport into the brain?

Yeah, such a good point. And you know, I go back to, you know, when I learned medicine, which was way back in the 1970s and 1980s, the idea was make a diagnosis or write a prescription or send to surgery.

And the new medicine has changed that dramatically. As you know, we now need to understand physiology. What are all the things that play into this problem?

So here's the issue with insulin. So what happens is normally your brain requires one of only two things to have its energy, because of course, it's got to have the blood flow or the oxygenation, but it's got to have as substrates, either glucose or it's got to have ketones.

And what happens, unfortunately for so many of us as we get over 40, both of those fail. So when I see patients who have cognitive decline, to me that is an energetic emergency.

They are sputtering on the energy. And here's why. What happens is because of processed food, because of high fructose corn sirup, because of high carb diets, unfortunately, because of low fiber diets, all these things contribute.

You now develop this insulin resistance. And in fact, what's amazing, you can actually see it biochemically. So the insulin receptor interacts with a signaling molecule called Iris one and iris one has different phosphorylation sites when it's active, when it's signaling, it is phosphorylated on Tyra's scenes, but when it is now resistant, when it's now shutting down and saying, okay, don't bother me, you've been pushing me too much, it's phosphorylated on serine and threatening.

And so some beautiful work out of UCSF showing that for people with Alzheimer's is you always see this push in the brain toward the searing three and so literally toward insulin resistance.

So unfortunately, because of these high dyes, your insulin is going up, it's signaling like crazy. And finally, it's a little bit like if you are listening to music that's too loud all the time, you just put earmuffs on.

You say, I'm not going to listen to that anymore. And so then of course, your spouse comes in and puts on a bronze lullaby. You don't even hear it. So what happens that shuts down the ability to utilize glucose optimally?

What happens? Will you still have ketones, right? No, you don't. Because what happens is the high insulin prevents you from making the ketones. So when we see patients, we have to restore both of those, which is, as my wife points out, Dr.

Aida LESHIN, who's been so fantastic about showing us, you know, how this is all working together. As she points out, you have to have metabolic flexibility.

So we are trying to do both. We try to restore the ability to utilize glucose, but we also restore the ability to produce ketones.

Amyloid, Estradiol, and Brain Signaling

And often we start because of this emergency, we just give some exogenous ketones, at least have something to get that brain going again. And then over time we want to make you insulin sensitive and then ultimately make you be able to make your own ketones, have endogenous ketosis instead of XYZ and as ketosis.

And that's the way the brain works best. And we see it again and again. People just come back to life. Their spouses say, Wow, there's so much more engaged.

They're able to do things. They're able to remember things that they couldn't before. So absolutely, insulin resistance is one of the most common and most severe problems when it comes to risk for cognitive decline.

That's so critical because so many people think just eat a high fat diet, it'll fix everything. You know, there is no easy panacea to that. You've got to get back to basics.

Like you said, you know, you've got to fix that insulin resistance. And you keep talking about energetics, which is so interesting, mitochondria. So maybe you could tell not everybody knows what a mitochondria is.

And it just as a side note, estradiol is really key to mitochondrial function. I always have to throw that in. But can you explain like what is a mitosis, Andrea?

And and how is that so important for brain energetics and what does that really mean, having energy in the brain, what is the brain even doing exactly that it needs energy.

Yeah. So again, you know, you bring in the blood flow and the oxygenation, that's a little bit like filling your car up with gas, but something's now got to use that gas.

Some things now actually have to make the energy and that's where the mitochondria are so critical. Some people say they're like batteries in your cell, but they actually do much, much more than that because they participate in calcium signaling.

They participate. They actually have their own little genome. They just do so many amazing things. And unfortunately, they can be damaged as we age. And there are a lot of mitochondrial toxins out there, unfortunately.

So you want to keep your batteries in good shape, you want to feed them appropriately and you want to keep them, you know, humming because having them optimal working optimally is so critical.

So energetics. Absolutely. And of course, it's turning out that energetics are important not just for Alzheimer's, but for other neurodegenerative diseases.

And now, as Dr. Christopher Palmer from Harvard has shown recently in his book Brain Energy, they also turn out to be important for psychiatric illness as well and other illnesses as well.

So unfortunately, this is something that is commonly a problem that can lead us to these complex chronic illnesses such as Alzheimer's. And another good example you look at Parkinson's.

Parkinson's is really related to the reduction in one complex, which is called complex, one of the mitochondria, if you take a complex one inhibitor over time, you will develop Parkinson's disease.

So we know that these things play a crucial role in many diseases. They are important for energetics, but also for buffering and also for all sorts of cellular signaling.

And they interact with the rest of the cell. As has been pointed out, these are were originally bacteria, many, many, many, many millions of years ago that invaded and end up becoming part.

It's almost like there's a wonderful kind of employer employee relationship or more, I would say more collaborative relationship where they're working with your cell, they're providing the energy your cell is providing them with the substrates, etc..

And so this is why it's so critical to have your mitochondria functioning, hitting on all cylinders, and to have the appropriate ability to go back and forth between burning ketones and burning glucose.

So I've heard some terms like mitophagy or mutagenesis. So what if you've had a lot of damage to your mitochondria? Is there hope to get them back online and working better?

Absolutely. And so you mentioned Milo Genesis in Mitophagy. So what happens is we recycle cellular components and so mitochondria, as they get worn down, get essentially dismantled and the parts are used once again.

And so Mitophagy is essentially eating the mitochondria, dismantling them, cutting them up, and then you can use the parts once again and there is and there's mitosis genesis.

And by the way, things like PCU can enhance your might of Genesis as can things like cold plunges and things like that. So you can make more to mitochondria and you can recycle and break them down.

Now, one of the interesting things, if you prevent getting rid of the old batteries, guess what happens? You develop Parkinson's. So it is critical that we do break these down as they become less effective and that we now replace them.

So, yes, there is hope. And again, doing the right things, getting on the right protocol, the optimal protocol for several months helps to kind of build these things up and improves the overall function.

Now, a lot of people have heard of Coenzyme Q10. That gets thrown a lot around. And you mentioned some different like items that may be related. So maybe you could just make a couple of comments on Coke, Q10, coenzyme Q10 and what can help promote it.

Is it important? Does it make sense to take a supplement of it now. Yes or no? I mean, so it's not it's not a cure, but it definitely can help your mitochondria.

So what happens is your mitochondria have this just absolutely beautiful pathway where they convert the food you eat, which is essentially a stored way to have things that are in a reduced state.

And what happens is you are literally taking these from a reduced state to an oxidized state and again accumulating the energy that comes. This is an oxidation reduction reaction, classical chemical reaction.

It's essentially saying and again, a little bit like a battery, it's essentially taking something that food that you're eating and saying, okay, those electrons in your food are actually wanted more by oxygen.

So we breathe in the oxygen. It's down here at the other end and it's going to as through one step, another step, another step. And Cocu, by the way, is is in there and is one of the messengers in those steps is slowly breaking down that food and ultimately handing those same electrons to the oxygen to produce water.

Insulin Resistance, Ketones, and Metabolic Flexibility

So it's a beautiful system whereby the oxygen is going to be getting these electrons, your food is going to be giving the electrons, and you've now captured the energy as it goes is a little bit like having a waterfall and capturing that energy as the water comes over the waterfall.

And so this is why, yes. Q10 One of the things and of course there are, you know, various cofactors things that I've mentioned like, you know, like giving people things that like still l-carnitine for example.

So there are, you know, the fat related, the oxidation and, and multiple ways that you can support these things. And so absolutely one of the most important things to do is to support your mitochondrial function.

And again, back to your energetics, make sure your blood flow is good if you've got vascular disease, it's important to address that, make sure that your oxygenation is appropriate.

Make sure that you're able to go back and forth between burning glucose and ketones. All of these things are important. You know, you talk a lot about vascular health and blood flow.

So they, you know, talk about vascular dementia. Sounds like there's not that much difference between vascular dementia and Alzheimer's or is that really a totally different condition?

It's a great point, you know, and it's a spectrum. So when I was training, we all learned to calculate something called a Kuczynski score. And that was supposed to tell you whether it's vascular dementia or whether it's Alzheimer's.

Well, guess what? It's turned out to be much more related than was thought. And it's very clear that in Alzheimer's, one of the earliest changes is changes in the blood vessels.

So there's no question they're intimately related. But you're right, there are people where it's really 90% vascular dementia and there's very little, if any, Alzheimer's, and there are others where it's more pure Alzheimer's with very little vascular component, as you could see, since we're talking about energetics and inflammation, you don't have to have a vascular component you can get.

There are many ways. And that fact, that's one of the things that we discovered and published a number of years ago. You can get there with chronic inflammation.

You can get there with hormonal laws, you can get there with toxin exposure, you can get there different ways. But vascular, a component from vascular already is common.

You can get there with some head trauma as well, things like that. So these are all important. This is why when we evaluate and treat people with cognitive decline or risk for decline that we want to prevent, we look at all these different variables so that we know what to address to get the best outcomes.

You know, it's so amazing when you talk about actually looking at what's going on in each individual, because I have patients that come in and they tell me their mom was diagnosed with Alzheimer's.

And I'll say, based on what they said, they just said. So, you know, it's like the person is clearly demented. You know, she can't remember anything and she is getting lost in her own home.

It's obviously kind of late stage. And they say you have Alzheimer's and it's like they didn't do a single test. It's just so amazing. And it gives me so much hope that people out there who are listening are going to demand the proper care. Right.

Like, don't assume anything. You've got to check it out. Right. Just find out. And one other thing I want to ask. So in terms of vascular so back way back in medical school, I learned about this thing they called the blood brain barrier.

And it's like, well, it's not really such a good barrier. So is there a function of like impaired blood brain barrier in the development of some sort of dementia or what the heck is the blood brain barrier anyway?

Yeah, it's a great point. You know, what happened many, many years ago? People were studying the brain and injecting in in autopsy studies and actually in animal studies, the injecting dyes and what they saw was certain dyes

would exit vessels in other organs, but not in the blood brain barrier.

So they knew something is different about the vessels in the brain than elsewhere. And what they found is that there are tight junctions there that are preventing this. However.

And so for years it was okay, things don't cross the blood brain barrier. It's turned out, though, that many, many cells and organisms and things like that have the ability to get across that barrier anyway.

And there was an interesting study done several months ago where they wanted to ask, okay, if someone gets a candidate infection and yeast infection basically, and the candidate gets into the bloodstream, how many months can you actually keep that out of your brain?

How good is that blood brain barrier? So they actually did this in rodents and they injected the candidate and they looked to see. And the surprise was the candidate crossed the blood brain barrier within minutes.

And then the response of the blood response inside the brain was exactly what you would predict. It was an early Alzheimer's like response. You're basically producing this amyloid that is trying to kill the invading organism.

So we've really had to modify the idea of what the blood brain barrier is sure for dies. It can exclude lots of molecules, but you have in many of these organisms that will get through very, very quickly.

Well, that is really such a revelation, because I know I was taught not that and I like, but I'm sure many of us older time doctors were taught that it really kept things out.

And so just recognizing, number one, the amyloid data is actually trying to deal with it in a beneficial way. But, you know, it's too much. It's too much and that infections so really kind of having respect for infections and what they can do and how they can get in the brain and then create this chronic state of inflammation and degeneration on all of this.

And I can't move into the therapeutics where I want you to talk all about all you learned about how to reverse Alzheimer's, which also applies to how to present it without touching on giving hormones to older women.

Most of our listeners are probably in the reproductive age group, but if many of them are older, we now know this was actually said by academics. I'm sure this won't shock you that PCOS disappears at menopause.

It's like, how can it disappear? You know, it's a metabolic dysfunction. Well, now they said, guess what? It doesn't disappear. It just sort of ends up blending in with all the metabolic dysfunctions of menopausal women.

Mitochondria, Mitophagy, and CoQ10 Support

It doesn't disappear, of course not. But in terms of the hormones, like I said, it endeared me to you forever that you utilized estradiol as part of your protocol.

So I can't let anyone leave this interview without hearing what you have to say about giving estradiol for brain health in older women. And you know, this whole thing, it's like going to give you dementia.

I know you people have heard this now from the Women's Health Initiative, that estrogen gives you dementia. I mean, it drives me crazy. So can you just say a few words about estrogen, estradiol, maybe conjugated equine estrogens, the brain and menopausal women?

Because whether you're in menopause now, ladies or not, you're going to be. Yeah, it's such a good point. And again, we're only interested in one thing best outcomes.

How do we get people to prevent and reverse cognitive decline? And we've seen such wonderful results. In fact, there's a whole book that I actually wrote with seven of the survivors called The First Survivors of Alzheimer's, and

they wrote their own stories.

So it turns out, if again, if you look at what gets the best outcomes, that must include optimizing hormones. And as I mentioned, you can you know, you can see the biochemistry beautifully.

The estradiol literally signals to your AP things good. I mean, I cut you at one site and I'm going to generate these two peptides that will now help grow and maintain synapses. And as anyone doctor Anne Hathaway is someone I work with frequently, for example.

But anyone will tell you who works with patients with cognitive decline and and has had wonderful results and along with Dr. Kattouf and Dr. Deborah Gordon worked with me and we all published together the results of our clinical trial last year.

The women always do better when they have bioidentical not just HRT, but bioidentical hormone replacement therapy. Now, of course, this is an area of great controversy, and I don't pretend to be an expert in it.

I'm interested in cell signaling and how we make people better with their cognition. But experts like you and Dr. Hathaway will decide, when do you want to do this?

I recognize in a best case scenario, you want to start, you know, right around the time of menopause. But she's found that even people who are much older are still getting benefits from be HRT.

When used appropriately and optimally. So again, I can't argue with the data. People tend to do better. Now I know we keep getting these things starting with the W. H.

I read even more recently, oh this is a problem. But these are typically the wrong molecules. You're trying to use something that's not bioidentical and then you're coming to a conclusion, Oh, you shouldn't be doing this.

Well, you shouldn't be doing it with that molecule. I think we can all agree on that. But depending again, depending on patient by patient, for most people, they do better.

When you include this as part of the overall protocol, we have to remember this is a precision medicine approach. This is not one size fits all. So we're looking if you have certain pathogens, take care of them.

If you have certain toxins, we're going to address those. If you have a leaky gut, as you mentioned earlier, if you have a poor oral microbiome, in fact, the pathologist show us those organisms from the oral microbiome such as P gingivalis are found in the brain of patients with Alzheimer's.

So that's what the amyloid is all about. It's literally sequestering them and killing them. Now, one critical point I want to mention before we finish here is that there are four stages, four fundamentally different stages when you're developing Alzheimer's.

And if everyone simply remembers that get in early, then we'll have very little dementia. That really doesn't need to be a lot. So stage one, you are asymptomatic.

And so often people, even in their late twenties, in their thirties, you can already show beginning changes. If you do PET scans or spinal fluid. Now the great news is who wants a spinal?

I don't want to have a spinal tap every year. The great news is there are now blood tests. One arm is already on the market and available is called p tal 181.

This is exactly what I was talking about before. This is telling you. Aha. Your AP signaling is the bad side. Now if it's starting to go up. Okay, great.

The earlier you get in the better off you are. So stage one is asymptomatic. Stage two is called MCI subjective

cognitive impairment. You know there's something wrong your spouse may know, but you're still able to score within the normal range on standard cognitive testing on average, as the epidemiologists have shown us that last ten years.

So in fact, you have a tremendous window of opportunity so we recommend everyone who's 40 years of age or over, please get evaluated, get a cognitive copy, which is again, we all know to get a colonoscopy when we turn 50 and if you're 40 or over, get a cognizance copy.

And if you're 65 and you haven't got one, don't worry, get one. Now get checked out. That looks at blood tests. It looks at a simple online cognitive assessment.

And then if you're having symptoms, you want to include an MRI with volume metrics. But if you're not having symptoms, just the first, you don't need the MRI.

So that's the second phase. Those two phases are 100% treatable.

Vascular Health, Blood-Brain Barrier, and Infection

The third phase is now called mild cognitive impairment. It's unfortunate that they chose the term mild. It's like telling someone, please don't worry, you only have mildly metastatic cancer.

It is a relatively late stage of Alzheimer's disease. But the good news is in our trial, 84% of those people improved. Now, unfortunately, many of them didn't improve all the way back to perfect, which is why I say, please get in on those first two phases.

But if you do develop the third phase, don't give up. There's a lot that can be done and we can improve you most of the time that each year those people with MCI and that the definition of that is now you are scoring abnormally on cognitive tests.

Each year, 5 to 10% of those people convert to the fourth stage, which by definition means you've begun to lose your activities of daily living. That is dementia.

That is the concern we all have. We don't want to wait for dementia. We've all just heard now about Fiona Philips from the UK, who has just announced that she's been diagnosed as having old timers.

Unfortunately, many, many celebrities, especially will wait and wait and wait and wait. When you want to do the opposite, get in early, address it early for best outcomes.

You then don't have to progress to these other phases though. In this final phase of dementia, you lose the activities of daily living, as you know, and now we do see some of these people improve, but it's harder and harder, no surprise as you get farther and farther along.

So if we could just get everybody to come in early, things would be so much better. But of course, the doctors have done everything backward. We've told our patients, oh, it's probably normal aging, you know, don't worry about it.

You know, if it's Alzheimer's, there's nothing we can do anyway. So don't worry. And people wait and wait and wait. We need to convince them to come in as early as possible, not as late as possible.

And in fact, the outcomes will be so, so much better. Well, that was so important for everyone to hear that there are different stages and that you can completely reversed in the first two.

So let's assume because our audience is women with PCOS primarily or health care providers that are taking care of them, that we now know that women with PCOS have many of the risk factors for developing Alzheimer's, just like they have risk factors for having cardiovascular disease.

I mean, know your risk. So then you can take proactive steps. So let's assume everyone listening is either caring for or themselves have these risk factors and they're maybe in stage one or maybe two.

And, you know, we'll leave that the other ones, you know, for like dealing directly with the health care professional. But what in terms of all you've researched, where should they start?

How are they going to reverse what may already be happening? But they don't even know it because it's asymptomatic or it's not really very perceptible, but they just know they're not quite the same as they were before.

So what are the positive steps like? Tell us all. Yeah, great point. And so we developed a prevention program called Pre-Code Prevention of Cognitive Decline and a reversal program called Recode Reversal of Cognitive Decline.

And what this consists of is two pieces. So you have the core because you know everybody you want to do the basics. And that consists of seven things.

It's diet, exercise, sleep, stress, brain training, detox and some targeted supplements. And each one of these things has very specific things, which I outlined in the book, and we also have it on the website, etc..

So you can see what are these critical pieces you need a plant rich, mildly ketogenic diet. That's what works best for getting you to be insulin sensitive, metabolically flexible into mild ketosis.

Each of these things, again, there's specifics for exercise. One of the things I love is called what exercise with oxygen therapy really helps getting oxygenation, getting the energetics to the furthest reaches of your brain.

So those seven basics. And then beyond that, you want to have the evaluation and look to see do you have specific pathogens? They could be coming from your mouth.

You may need to go on dental side and for example, you may have an undiagnosed abscess which can be seen in cone beams, for example. You may have a leaky gut.

Just as you mentioned earlier, we see a number of people that will have chronic infections they're unaware of, often from tick borne illnesses, but Beja, Bartonella, Borrelia, Alicea and a plasma, all those sorts of things they don't even know they have them.

They just know that their cognition is not what it is. They've often got some brain fog. We root those things out, find them and get rid of them. Because again, your amyloid is basically saying, hey, you haven't gotten rid of this problem, so I'm just going to sequester it and I'm going to try to kill it and kind of put it off to the side.

Well, after a while, you've got more and more of this stuff all over your brain. And so unfortunately, when you have an inflammatory state, these things literally it's like a fort with soldiers that have got cannons and it opens up and is letting out the guys that are not good, that are now spewing all this stuff around and unfortunately damaging your synapses.

So you want to look at those things and then toxins and the toxins come in three varieties. It's the inorganic things like air pollution, which has turned out to be very important as a risk factor for Alzheimer's.

So again, great. Just good living. So helpful. Get out of the house. You get out into the clean, fresh air. Get down to to the ocean where you get some nice, clean, fresh air or two legs or wherever you like to go.

That's got great fresh air. And then of course, in the inorganic is also mercury and some of the heavy metals. Number two is the organics, things like glyphosate, toluene, benzene, formaldehyde, all of these things.

And of course, they are part of your toxic burden. And then the third group is bio toxins. And these is really unfortunate. Unfortunately, as you know, many of us live in homes built of mold, food built of, you know, wood that

got wet.

Hormone Therapy, Stages of Alzheimer's, and Early Detection

And unfortunately, we've got mold living and we hear this all the time. I just heard about another patient earlier today, just huge, huge levels of these mycotoxins that are so damaging, they damage your nervous system.

They damage your immune system. They damage your kidneys. They can be associated with increased risk for cancers. So, you know, this is a really this is a really tough thing and important, again, to to just get out, get away from this stuff and you can easily have your home evaluated.

So it's those two things. It's the seven basics and then it's the specifics. Let's find those things that unfortunately the vast majority of doctors are not doing the right tests and they don't know how to treat this, which is why you hear people say every day Alzheimer's is untreatable.

No, not at all. We've published very good results. We've got published the best results in the world. So far. And I have trained over 2000 physicians from ten different countries and all over the U. S.

to do this protocol. And of course, it's a little bit like learning surgery. Some of them do it better than others. Some of them do it well. Some of them do it not so well.

So good to know, you know, how successful your doctor has been. If the doctor is a trained doctor with other patients who had cognitive decline. So, yes, I agree with you.

And I would urge everyone, please get on active prevention or early treatment. I know a lot of times you people go in and the doctor will say, oh, you know, what are you here for? You're not doing that badly.

Well, yeah, the doctor should be saying the opposite. Thank goodness you came in early and you didn't wait until this was severe and there was less that could be done.

Well, the you mentioned the word precision medicine. I think that really says it all. You can't assume what is going on. You've got to really check it out.

And you need someone that cares enough to learn how to to investigate the problem. And I just would like you to elaborate just a little bit on the topic of that mildly ketogenic plant based diet, just so that people would have an idea of what does that mean you're eating for breakfast, lunch or dinner.

Yeah, great point. And by the way, you can actually order this. So we actually worked with a company called Nutrition for Longevity and they now actually can deliver this.

So the easiest way to do is go on keto flex 123. com and you can actually order these and they'll bring them to you as very easy. But the bottom line is again, it's all about getting the optimal biochemistry.

And what has worked the best so far is this what we call keto flex 12, slash three. This means it is a flexitarian diet. So if you want to have fish and meat, great, make sure it's wild codfish, low mercury fish, make sure it is grass fed beef or make sure it is pastured chicken, pastured eggs, things like that.

And if you, on the other hand, you want to be a vegetarian, no problem. Just make sure you're doing okay with your vitamin B12, your vitamin D, make sure you're getting enough choline and things like that that are all important either way. Good.

But you want to get yourself into that again, metabolically flexible state. Now one one paradox important for everyone to remember. So many people say, well, you know, I can fast now for 20 hours, be careful.

Remember that Alzheimer's is ultimately a network insufficiency. There's not enough support, not enough blood

flow, not enough oxygenation. So if you starve yourself, you can actually hurt yourself and go backward.

So you've got to be careful. On the one hand, you want to become insulin sensitive. On the other hand, you don't want to starve yourself to do it. So you want to ease yourself into that over several weeks.

And so, you know, the things that you eat on that are large cells. So what I like to use myself and again, you know, I love eating these with my wife, who is incredible at making these amazing, wonderful salads.

And of course, I do it as well, but not nearly as well as she does. She is a fantastic physician who gets this and really taught me a lot of this. And so it's going to be you know, you might like romaine lettuce, you might like a regular grape for your nitric oxide, by the way, that you mentioned earlier.

Then, you know, it's it may be some a couple of eggs, hard boiled eggs, not overcooked, hopefully. And and then it may be some beans. It may be a little fish.

It may be, you know, all sorts some carrots. It may be some beets. You don't want to overwhelm yourself. Beets can be somewhat sweet. I mean, these are infinitely variable.

So that's the sort of thing I like. You may want to have more of a classical dinner, for example, or or supper or even late lunch. And so you might want to have a piece of salmon and you might want to have some asparagus, which is wonderful right now.

And again, you know, organic, local, always the best. You don't want to have a lot of mashed potatoes. You don't want to have a lot of bread. So what we try to avoid is simple carbs, grains, because so many people are sensitive to grains and it can induce leaky gut.

Of course, for so many of us you want to avoid standard dairy, A1 dairy can be a big a proinflammatory problem for so many. Just as you indicated earlier, people who are taking oral estrogen bad idea can be inflammatory.

And so those are the sorts of things that you can eat that are, you know, delicious, fulfilling have all the all the great stuff in them in a good to your gut you want to include also some probiotics.

So you may want to have some things like, you know, like fermented beets or like for or like sauerkraut or things like that. Probiotics, prebiotics and post biotics.

All helpful. And then of course, good idea to check your gut and see do you have leaky gut? Do you have SIBO? SIBO is turning out to be so common and can really be a problem.

So you know, again, we're realizing that human physiology is so complicated.

Prevention Protocol, Diet, and Resources

But the good news is we can see patterns where we can address these things and make it so that virtually nobody needs to get dementia associated with Alzheimer's disease.

Well, that is so reassuring. And just how much we have in common. I created, but I didn't really create what I call the breakfast salad, you know, like these because you have to have the engage.

I know. You know. Yeah. Like start your day with this incredible breakfast salad with all the kinds of things that you mentioned. You'll be full for so many hours and you're getting all those polyphenols and fibers and antioxidants and you know, everything.

So we have barely scratched the surface and everyone wants to read in detail about the different supplements and your regimen. So how can they find out more about your research, the past research, the ongoing research, future research, the different books, publications so they can really know what to do for themselves and for their family

members.

Great point. So I published three books. The first one is called The End of Alzheimer's, came out in 2017. It's now available in 33 languages. So whatever language you like, it's likely to be available the second one.

And then what happened at the first one, people said, Well, we want more details, you know, really, you know, really drilled down into the specifics. And so actually I worked on this with Julie G, one of the patients who's done extremely well is going from the 35th percentile to the 90th percentile.

She's sustained her improvements for over ten years. She's done great. And also my wife that I mentioned earlier and the three of us wrote the second one, which is called The End of Alzheimer's Program.

So this is now the program to go on. And then the third one is the one I mentioned earlier, which is The First Survivors of Alzheimer's. And I have to say, for anyone who reads that, seven different people who write their own stories watching their parents pass away from Alzheimer's, being told that they're going to go the same direction and then getting better.

If you can read that without a tear in your eye, I'm impressed. You know, you're pretty tough person because they are amazing and beautiful, beautiful stories.

And of course, one woman talked about looking at her own children, realizing she, you know, she has the gene. The children had the gene. Oh, my gosh, what's going to happen to them?

And she's recovered beautifully and now really realizing we've ended it with that generation. You know, we should be able to end this disease with this generation.

So those three books, you can also go on DrBredesen.com You can also look at Facebook, which is Dr. Dale Bredesen or Instagram or Twitter. And then perhaps most importantly, we are now establishing the first place in the world that people can come for hope for neurodegenerative diseases.

And this is called Precision Medicine Program for Neurodegenerative Disease. And this will be at the Pacific Neuroscience Institute in Los Angeles. So I'm very enthusiastic about that.

For the first time, we'll be able to get these larger data sets that are needed. The other thing I should say is there is a documentary that's been made on this work by NHK, which is the CNN of Japan, and it's now circulating around.

It just played at the Manhattan Film Festival and it's circulating around. I think it's going to play in Charlotte in September, Charlotte, North Carolina.

So it's going around it. It's called Memories for Life, Reversing Alzheimer's. So if you get a chance, you can check that out as well. Well, this is really a story of hope.

And I just always emphasize, know your risk, low risk is not destiny. But if there's one thing that you have proven is that there is no destiny to have Alzheimer's no matter what your ancestor was have or where you are even right now in the vast majority of cases.

So destiny is what you create, right? And know your risk and then read these books. And I can tell you, you just be prepared and know I'm in Orange County.

I'm going to come and visit. Okay, great place and stay up on all of this. This is such amazing, groundbreaking work. Thank you for all you have done and everyone out there take action today.

Do the things you can do to keep your brain working. Well, in fact, I know I've read that the thing is feared the most is in a heart attack isn't cancer, it's dementia.

So we can do all of this. What a story of hope. Thank you again so much coming and joining me for this interview. Thanks so much, Felice, for having me.

Great to talk to you.