Dr. Bredesen: Hi, everybody, I hope everyone's doing well. Now that the pandemic is on the decline. Great to talk to everyone again. We have two fantastic guests today. We have Dr. Kat Toups and then we have Julie G of course, as always. Julie great to see you, and Kat, thank you so much for joining us.

Dr. Kat Toups: Happy to be here, thank you.

Dr. Bredesen: And I want to get into discussion with Kat, especially, because Kat has a unique qualification. There are very few physicians who have both training in functional medicine, have practice of functional medicine for years, but on the other hand have also conducted clinical trials. And Kat, I know you've been involved with many, many trials and so you've got that unique combination. And tell us, how many trials have you been involved in, clinical trials?

Dr. Kat Toups: Right, thanks. Well, I used to run a clinical trials research center and I'm a psychiatrist by training, and also formerly boarded in geriatric psychiatry. So I did a variety of clinical trials, over 100 clinical trials in the 12 years that I ran my center, primarily in all areas of psychiatry, including Alzheimer's and MCI. Actually MCI was a brand new thing back then, but I've done 20 long-term trials in Alzheimer's and MCI. So some of them were multi-year trials.

Dr. Bredesen: Fantastic, so we want to talk extensively about the trial that we all just posted recently, because it really changes the game, it really changes a lot of things about the way people think about Alzheimer's. But as we've talked about before, we really need to kind of rethink everything in cognitive decline, because everything has been backward because people are just looking for that one pill, they want to wait 'till late stages. So one of the points I wanted to make is that we think of this as four separate stages. We think of it as pre-symptomatic, there's a stage where you can pick it up on PET scan, you can pick it up with spinal fluid, but there are no symptoms yet. And that's currently called pre-symptomatic stage. It really should probably be called pre-Alzheimer's, just like we talk about prediabetes, this is pre-Alzheimer's

because you've already got the biochemical processes going on, you just don't have a diagnosis yet. Then what we call talk about is SCI, subjective cognitive impairment, it should really be called early Alzheimer's. And that goes on for about a decade, because people will just let it go by and say, oh, this is really nothing important. But if they realize this is early Alzheimer's, this is where you're moving along. Now. what's interesting to me, what we call mild cognitive impairment, that's the third out of four stages. So this is a little bit like saying to someone, you've got cancer, but it's only mildly metastatic cancer. Well, that's a late stage and that's the same thing with cognitive decline. So I know in the trial, out of the 25 people that came through, 22 of them had this MCI, which I would argue should be called advanced Alzheimer's because it's relatively late, it's the third out of four processes. And then Alzheimer's itself would really be called the final stage. And we had three with dementia, three with all a full-on Alzheimer's out of those 25. So you talked a little bit about the trials, and I know these things take a tremendous amount of time, to get everybody to come in, to recruit the people, to get IRB approval. And in fact, we were turned down for IRB approval in 2011, we were turned down again in 2018, and finally accepted in 2019. So what would you say, just ballpark, How many hours would you say you have spent on this clinical trial? Dr. Kat Toups: I'm not sure, I know it's a lot. I'm not sure I want to figure that out, it's definitely been a multi-year process with a lot of love and passion to make this trial happen.

Description of the Evaluation and Treatment

Dr. Bredesen: So let's talk for a minute about some of the things, so to begin with, of course we flipped the script, you evaluated the many things that were actually driving the cognitive decline, as opposed to the old fashioned approach, which is currently in use everywhere else, where you just predetermined we're going to give you this drug or this instrumentation or whatever. So if you could talk a little bit about some of the things that you evaluate on your patients who come to you with cognitive decline.

Dr. Kat Toups: Well, I don't want to take up our whole time here-

Dr. Bredesen: It's a lot, I know.

Dr. Kat Toups: We look under every rock. There's so many factors that can affect the brain. And many of them are well-known with nutritional deficiencies, the B12 deficiency, the vitamin D deficiency, if you have diabetes, if your blood sugar is out of control, these things are pretty well known. But I think some of the things that we looked at that was different than in other trials, that many, many people miss are the role of infections in the brain, which we're learning about from COVID. But people in our world already knew about this, the lack of hormones and that effect on the brain and then the toxins. And of course this is becoming an increasing factor with our world becoming more toxic, that the toxins were, learning more and more that those things really are triggering events in the brain. So we did quite a variety of lab testing. We did sleep apnea testing. We certainly know that sleep apnea is a big factor. And one thing that I like to stress with sleep apnea is you do not have to be a big burly man with a thick neck, the typical classic sleep apnea. I find sleep apnea in thin women. So in my mind, everybody needs to be tested for that. And that is one of the things that we looked at in the trial. So quite a few things that we tested.

Dr. Bredesen: Absolutely. And then when you targeted these things, obviously one of the goals here was to bring them not just to the lowest range, but actually to an optimal range. And maybe you just spend a minute talking about some of the things, I know you actually were amazing because you actually had your patients, you actually had a group where you would have group sessions and make sure that everybody was doing the right things, which I think really helps as a way for people to share information and you've got some tremendous results. So please talk a little bit about what you did for your various patients in the trial.

Dr. Kat Toups: Yeah, well, that's the $50 million question because there is no one thing that everybody did. Now, we had some certain parameters in the trial, everybody needed to exercise, and we had a prescription for exercise.

Pretty much we'd like to have people think that exercise is a daily factor of life, right? I tell people your goal needs to be seven days a week, because something's going to happen one of those days. And if your goal is four days a week, and something happens one day, you're down to three days a week. So exercise was, I feel like it's one of the best validated things we can do for our brain. So our patients actually had, they consulted with an exercise coach who helped them all. And I found having that exercise coach was a huge factor for my patients that I hadn't really utilized before. And there were people that had never, I had a patient that had never exercised ever in his life. And he ended up loving exercise from working with our coach. So they had to exercise every day. And that was a combination of strength training and aerobic training and high intensity interval training. They had to do brain training every day. We want to remove all the factors that are triggering the brain, but then we have to rehabilitate the brain and use neuroplasticity to get things to come back. The exercise is part of that. We use BrainHQ Brain Training, and our patients were required to do that six times a week. We know that meditation can change your brain and also increase your brain derived neurotrophic factor. So we incorporated HeartMath as a mindfulness, meditative kind of component. It was something that could be standardized, that everyone could do. Obviously, there's many forms of meditation and mindfulness, but we needed to pick one that everybody could do and that we could monitor. So we incorporated all those things and we made sure they were sleeping. We made sure their sleep apnea was corrected. And then we did a big panel of testing and also including immune testing, I don't think I mentioned that, because we know that it's the immune system reacting to triggers in our brain that are causing the neurodegeneration in there. So we got a big panel of labs on everyone, and then it was put it together, what are the factors for that individual person? So that's where it differs for every person, what factors do they need to do? And I didn't mention the diet, of course, I think most people know by now the diet is pretty primary. If you're not on a good diet, you can just hang it up, right, that's where you start with everything is a nice, clean diet. And we worked hard with our patients, fortunately, I live in the San Francisco bay area and there is a high awareness of the role of diet and nutrition. And so many people came in with a pretty good diet, but we did work with that as part of our study protocol. People were asked to use a ketogenic diet, obviously a whole foods, primarily vegetable

based diet, meat as a condiment, if they were eating meat. And we did ask them all to get into mild ketosis and we help them with that.

Dr. Bredesen: And talk a little bit about low dose naltrexone, how did you decide what people to give that to and what people not to give that to?

Dr. Kat Toups: Yes, so low dose naltrexone or LDN, as we call it fondly, is a compounded medicine that when we put it in little tiny doses, it temporarily blocks our opiate receptors, and that causes our brain to make six times more opiates. So it's an interesting thing, because opiates are feel good hormones and I've seen that help depression and anxiety. But those opiates then bind to your T regulatory immune cells. And they cause a cascade that can help people with immune disorders. So for my patients in the study, I did have a handful of them taking LDN and I was screening for a number of immune factors. So we look for ANA, we look for thyroid antibodies, we look at an immunoglobulin panel. Those are kind of some of the first level of screenings for the immune system. And if we start turning out markers that indicate that there is some auto-immune factors happening, we definitely incorporated LDN for those patients.

Dr. Bredesen: Can you talk a little bit about, if you would about a number of people had various toxicities, for example, biotoxin, some people had mycotoxins, and what did you do, these are often the most difficult ones to treat. So could you talk a little bit about what you do for people who have mycotoxins?

Dr. Kat Toups: Yeah, so mycotoxins are from mold, I think a lot of people are familiar with that term, mycotoxins, but it's not the mold itself, but it's the spores that it gives off that can cause problems with people's health. And we know that certain species of mycotoxins are more problematic for the brain. And it's clear that some of them are a part of a neuro-degeneration picture for people. We see even young people with problems with mold exposure, who get very bad brain fog and cognitive issues. So all of our patients did a mycotoxin, a urine mycotoxin screening panel. And that would give us some idea of what was there, when there were markers indicating that things were

high or we got a history that there was leaks in the house or water damage or visible mold. There were some people in the trial that lived in places with quite horrific, visible mold. Then we asked people to do some testing of their home. So with the mycotoxins, what we tend to do is first we try to remove the source. We try to figure out where are you getting exposed to this? And let's try to fix that problem, which was a huge problem during our trial. Because two of my patients found, we had testing, and they had mold in their home. They needed to do some cleanup and remediation. And because of the early COVID lockdown, no workers were coming into anyone's homes. So they had to shelter in place in their home that was moldy. And we could see the effects of that on their testing, actually, both of those patients made a big improvement at the three month mark. We tested, this was a nine month trial, we tested our patients at baseline, three months, six months, nine months. So these two particular patients of mine had improvement at three months. And then we had lockdown and then they both had a decline. Now one of those two got in gear while she was there, she started getting rid of everything, cleaning up everything in her home. And she actually finished with a perfect MoCA score of 30 by the end. So if you're doing things, and then of course, as far as treatment with the mold, one of the important things we do after trying to remove the source is we want to bind up those mycotoxins in the body. So we use a combination of different binders for people, cholestyramine, activated charcoal, clay, things like that. And then we also will tend to give liver support to help the liver that's our master detoxifier organ.

Discussion of Clinical Trial Results

Dr. Bredesen: Yeah, great point. You had, I shouldn't mention, you had two of your patients who started with MoCAs of 19, so they're pretty significantly declined, both achieve 30, which was kind of amazing. So you had dramatic improvements of these people, basically to a perfect MoCA score.

Dr. Kat Toups: Actually one was a 29, but a 29 is pretty darn perfect.

Dr. Bredesen: At his final, but he had a third before that. He had a 29 at final, be he had a 30 at six months, So they both achieved a 30 during the trial,

which is unheard of. So congratulations on that. So let's talk for a minute about the outcomes. So we looked obviously at MoCA scores, we looked at CNS vital signs scores because that's even more sensitive. So they really complement each other because they have different dynamic ranges. We looked at MRIs, looked at what's called an AQ change score to look to see whether their significant others or spouses or study partners felt that they had improved. So if you could just say, and let me just put this in perspective, Donanemab, which was the one that Eli Lilly touted as highly successful recently, what it did, was it didn't make people better, it didn't make them stay the same, but it slowed the decline by one third. Now, in contrast, in the trial here, what percentage of the patients actually improved?

Dr. Kat Toups: Oh, in our trial, yes, 84% of our patients improved in the trial.

Dr. Bredesen: Yeah, so we've got one doing this and we've got the trial here doing this. So very striking improvements and improvements in MoCA scores, improvements in CNS vital signs scores, improvements in this AQC change score. So in fact, not only did they get better, but their study partners noted that they clearly got better. And interestingly, one thing you can't fake is an MRI. And so these people had very interesting MRI volumetrics. And I don't know if you want to talk a little bit about their gray matter volumes and their hippocampal atrophy which is again, characteristic of Alzheimer's disease. How did they do there?

Dr. Kat Toups: I can't remember those precise radiology statistics off the top of my head, but we were really shocked to find that in an only nine months trial, that for a few of our patients, even on their regular MRI, we saw changes in the MRI, which was completely unexpected. And then the volumetrics, we used a program called NeuroQuant that gives us a volume of each of the brain structures compared to somebody of the same age. And we definitely again found some unexpected benefits there in the gray matter and the hippocampal volume compared when we brought in our neuro-radiology professor consultant that compared them to statistical values for people. And the gray matter, both of those markers are expected to decline historically, even without Alzheimer's, just with age. And it was the gray matter, actually,

increased in our patients. And we would expect with normal aging, even over a year, that that gray matter would decrease. And of course, if you had MCI or Alzheimer's, it would decrease quite a bit more. So we actually had improvements over normal aging in our study, which of course coincides with all of the other incredible things that we saw happen. We saw people that had prediabetes, early diabetes, completely reversed that. We saw people improve their lipids, I had certainly one of my patients that came in on a statin and halfway through the study, his cardiologist said, no, you don't need to be on a statin anymore because he had reversed all of his metabolic factors. So what's good for the heart and the rest of the body is what's good for the brain. And we saw improvements across the board in so many things. And it was really exciting to see how fast you could move the needle. Take people with huge level of inflammation and bring it down. That people a hemoglobin A1C of like 5.8 or 5.9, bring it down to 5.1 or 5.2. We worked hard and fast and it was just so exciting actually to see when you go full court press that things can start changing very rapidly.

Dr. Bredesen: Absolutely, and that brings up a really important point. So Julie, let me turn to you, one of the big issues and we actually talked about this in the paper. And Kat, you brought this up over a year ago, you said, we're showing that this is possible, we're not showing yet that it's practical. And one of the big issues is okay, we now can show for the first time, we can reverse cognitive decline. Now we've published it before in the anecdotes, but the trial for the first time, gives us a denominator. So, Julie, I know you've been doing this now for nine years. If someone said to you, you can just go ahead and stop it because it's a real pain. What would be your response to that?

Julie: I have no desire to stop. I mean as you know, I not only was experiencing symptoms of cognitive decline, but I had many severe health issues. But I had many severe health issues. And pretty much all of those are gone now. And one of the biggest underlying drivers for me, was a Lyme Disease coinfection called babesiosis, which made me critically ill for 15 years. I mean, I was very sick. So I have no desire to go back to my previous life. I feel so much better. with a history of cognitive decline, I will be doing this for the rest of my life. And I don't see it as a hardship at all. And I agree with you wholeheartedly that we, as a team, have to work very hard on our

messaging, in simplifying the protocol to make it very easy for people to understand and make it widely available.

Dr. Bredesen: Yeah, well, it's interesting. I just was on a meeting yesterday with a guy who runs a number of assisted living places. And he said, once we understood and once we start seeing results from this trial, we realized we need to make wholesale changes in the way we deal with our residents. And interestingly, he had just started the beginning of the first piece, which was just the beginning of the diet piece. And already he was seeing big changes in some of the residents. So very exciting to see. And my hope is that we will really really impact the global burden of dementia over time with this. So Kat, let's come back to you for a moment and let's talk a little bit about what are your takeaways from this and what do you see as the next step?

Planning for the Next Trial

Dr. Toups: Well, my takeaways are of course, things that we already knew from working with this for so long, but I think now we have a quantification for people, we have some numbers to say, it's not just one-off patient with one doctor, we had three different sites, we had three different clinicians doing this protocol, and a majority of our patients got better. So the most important thing for me is always to give people hope, right? That when you have dementia and your doctor says, there's really, it's going to keep going. And when you believe that, you're sunk, you've lost the battle. So to me, the most important thing is that our study, I believe will bring people hope that this is worthwhile to do, because it's not easy to get started. But as Julie said, once you get in a rhythm, our patients did get in a rhythm, and they were able to complete all of our study protocols. And I had patients that went back to work, they had gotten better enough that they, had stopped work or weren't able to work as well. So you can do this with a regular life, as Julie said, I do it, she does it, many people do it. So I think the most exciting thing is just that now we have some numbers that we've tracked over time and not just case reports. So I hope the world will take notice and take hope from that. And of course the next step is we need more data. We need to keep doing this, we can refine the protocol. The hope is that we will, Dale already has a grant for us, the

people that kindly, I should say that the Four Winds Foundation, they funded our study, we're so grateful to them and they've agreed to actually continue funding. So the next steps are we're planning a trial with 100 patients instead of 25 patients. It will be done at an increasing number of sites. So we'll hopefully incorporate some different parts of the country and some different demographics in our study. And the plan is to have a control arm. So people will be randomized, either be in the protocol or spend a certain amount of time in the standard of care arm. We pretty much believe we know what will happen there, but we haven't of course, we're still trying to finalize all of our data from this study, but the thinking is that we might cross over some of the patients that are in standard of care, then cross them over to our active protocol and then look at what happens with that. We have a lot more to learn, of course we have a lot more, but things that we learned from this one will make us much more efficient in the next one.

Dr. Bredesen: Absolutely, and I think this next one, as you know, will probably involve eight doctors instead of three, because it's more patients and it takes time with each one. So there'll probably be eight sites around the country. So I hope that many people will get involved with this, it should be starting around the end of this year. We still have to get approval from the IRB, we still have to set up a number of things. And as you said, we're learning, there are new things that we're adding. And I think Julie, you've been involved with these sorts of things, as well. As you pointed out, you found out about the babesiosis, you also found out about plasmalogens, that made changes, you found out about katsu, that made changes. And the good news is, this is now starting to evolve. We now know we're headed in the right direction. So it's a matter of tweaking things here and there to get best outcomes, what sorts of brain stimulation do you want to include? What sorts haven't been as effective? One of the things we haven't talked about yet, is level of significance, because of course a big issue in science is was this statistically significant? And what that simply means is if you did nothing, and you'd had a random improvement or a random decline, what's the likelihood that what you did actually had no effect? And what you thought was improvement was simply by chance. So you can calculate that, is it 50%, is it 20%? What is it? And the usual acceptance in science, you want it to be less than 5%. So less than 0.05 is what people accept as significant. However, in this trial, the

significance for each of these things was much better than that, it was actually even much less than it was due to chance alone. And I know you did a lot of working with a number of statisticians on this, Kat, with determining what was significant, how significant and this sort of thing. So let me just mention that there was another trial that was published, in which they did a little piece of this, but they didn't look at some of the toxins, and they didn't look at some of the pathogens, and they didn't do some of the things that we did. And they actually did not see a statistically significant improvement. So I think it's critical to show that in this case actually there was quite high in terms of the significance, it was very low likely that this was just by chance

Dr. Kat Toups: We worked with a professor of neuropsychology with a statistical background looking at other dementia and cognitive impairment trials. And he was able to clearly show us that certainly it was not due to chance, that the different testing that we did with the MoCA, and the CNS vital signs, the battery of neuropsych testing, I don't understand how they calculate all the statistics. I'm a clinician and not a statistician, but it was pretty clearly shown that this has a high clinical relevance, a high statistical relevancy, and it was clinically significant. Okay, Dale, I'm seeing a questions come across. People want to volunteer for our next study. So I would say to people the next study is quite a ways down the road and there's no time to lose. So when you're having symptoms, you don't want to wait nine months to be in a study. Please don't wait for this study. And of course, when we have the study finalized and we do have the locations finalized, we'll be putting that out for people to know and recruiting. But as part of the study, half of the people are going to be on standard of care. So if you're having symptoms now, please don't wait, but we will certainly put out the information once we have the sites that are selected. People are going to have to live in that geographic area so they can actually come in for testing and we can support them in a trial, but please don't wait.

Dr. Bredesen: And it's probably going to be something like December, give or take a little, it could be January, but it's going to be something like that depending on how long the IRB takes to approve it and things like that. But as Kat said, there's no time to waste here. If you have any symptoms, please, please get on treatment immediately. There are now many, many people who

are able to provide this, over 2000, and we'll certainly announce it on this site as well as other places, if you follow Kat, or if you're a part of ApoE4.Info, all of these places will mentioning this. And another thing that I think is important to point out which is that this was a trial for people who had MoCA scores of 19 to 30. So they all fit the criteria for either MCI or for dementia. Nobody fit the criteria for normal. They all had issues, they all had issues with their scoring, but nobody had a MoCA score of zero. So I'm actually very interested in setting up a separate trial for MoCA scores of zero to 18, which would be the severe Alzheimer's reversal attempt. Now we have seen a few people and as I mentioned, I mean Kat had two people that went from 19 to 30, so there's no question it can be done. We have seen people who've gone from zero, but not to 30, we've seen people go from zero to seven, eight, zero to three, zero to five. And it makes a huge difference in their lives. They're able to talk again and dress themselves again and things like that. But no question it's harder and harder. And one of the questions is what do we have to do for people who are farther along? Do they need stem cells? Do they need intranasal trophic factors? What are the other things that we need to bring them back to the best outcomes possible, because of course, that's always the goal, what's the best outcomes? And then let's go back, Julie, for a second, I know the people who have been on ApoE4.Info, obviously, you're communicating with all the time. Do you have a sense for how many of them have said, I've been in a study before and the thing, the sorts of things that they did.

Julie: It's kind of sad, we've seen quite a few people go into studies and sometimes, especially, if they were part of a group that received treatment, we don't hear from them again. So I'm not sure what happens. On the other hand, the folks that are on the placebo side, stick with us. I'm not sure why, and we also do have a handful of folks who are in studies now, pharma studies.

Dr. Bredesen: Right, right, pharma studies. Yeah, and there are over 400 pharma studies that have failed and it's unfortunate, and maybe there will be one out there that will just be a cure. The molecular biology of the disease says that that's unlikely to happen, because you've got to hit so many different targets. But I do think part of the future is to combine these sorts of systems, medicines, and root cause approaches that Kat, and we should also mention Deborah Gordon and Anne Hathaway, two other physicians who saw the

patients. And as Kat said, The Four Winds Foundation who was good enough to fund it. And also CRO that worked with us on this, and Dr. Cyrus Raji, who is the neuroradiologist, and Alan Boyd, who was the one from CNS vital signs. So we had a lot of tremendous experts help with this. But I think that combining that sort of approach with targeted pharmaceuticals may well get even better results, we'll see. The good news is that this study showed unequivocally that people, the majority of people, who are in that 19 to 30 range, they clearly can get better if you do the right thing. So I think that's a critical milestone. Now, as Kat mentioned, the next milestone is, okay, let's take a randomized controlled trial with 100 patients and let's show the same thing. That we've seen now for years with anecdotes we've published, but now we've got the trial. Now we need a bigger randomized controlled trial. So let's go to a couple of the questions here. And then Janice says, HeartMath is excellent, I've stabilized high blood pressure with it. Hello from OKC, great, good, good to know, this is great. And so many of these things working, we've talked about wearables and some of these various things that you can do for yourself, so very helpful. And checking your ketone levels, just as Kat was talking about earlier Nicole mentioned, how many patients? And we mentioned 25 patients in this particular trial. Renee was asking, how can we volunteer? As Kat said, and yeah, please don't wait, just as Kat mentioned, If you do want to volunteer and you're at the right time, yeah, please just keep an eye. We'll make announcements at multiple sites probably in December.

Questions from the Community

Dr. Bredesen: Let's see, and Penny says, talks about her mother who's tried so hard for three and a half years and had small improvements. Yeah, let's keep optimizing for her. Sherry asked about trial patients being given fiber. Absolutely, this is a plant rich, high fiber, very much like what we've talked about is KetoFLEX 12/3, with appropriate fasting, appropriate autophagy, all of these things. And I dunno, Kat, do you want to weigh in about specifics beyond that? Anything else that you talk to your patients about with respect to their nutrition, other than plant rich with appropriate fasting and high fiber, high phytonutrient, mildly ketogenic diet, are there other things that you recommended to them?Dr. Kat Toups: Well, let me just say that I'm a huge fan of fiber. And I think it's pretty clear from studying some of the groups like

the Hadza Tribe and one the Amazonian tribes, that the people that eat 200 grams of fiber a day, which is unattainable for most mere mortals, don't have chronic diseases, right? They don't have diabetes, they don't have Alzheimer's, they don't have depression, they don't have heart disease, because of the lifestyle. So that's absolutely where we start with everyone. Each of our patients had comprehensive stool analysis testing, and we look at a variety of factors. The gut of course, is the root of your immune system. And you need everything functioning well to absorb your nutrients. And of course, many things are declining with age there. So I definitely had, besides eating a fiber rich diet, the first thing is, of course, how much good nutrients can you get from your food before you start adding things in? But I did have patients also on supplemental fiber. We know that fiber is a prebiotic and it feeds all our probiotics and getting the right mix of the probiotics controls all of the digestion. So that was definitely a huge thing. We all are trained in a model where first steps first, and you work with the gut.

Dr. Bredesen: Good point, and what fiber were you recommending, psyllium husk, or konjac root, or what sorts of things were you recommending?

Dr. Kat Toups: I think those are all fine. There's one a product that I personally like, it's called, it's from Master Supplements and it's on Amazon, not Amazon, I don't know if it's on Amazon, but it's on Fullscript and Emerson, and it's called TruFiber. And it's a soluble fiber and you can put two scoops in water and it just dissolves completely. It's easy to drink it down. You can drink it with the supplements that you're taking. So that's the one that I used if people needed extra fiber.

Dr. Bredesen: Yeah, and of course fiber and food is critical as well. And Julia, I just wanted to come back to you. When you first went from non-ketogenic to ketogenic, and got yourself into ketosis, what sorts of things, because people often ask me, is it really important to get into ketosis? From the theoretical side, it absolutely is, as Dr. Kinane has shown us over the years. What did you, as a person using this, What did you actually feel when you first went from non-ketogenic to ketogenic? And of course from insulin resistant to insulin sensitive?

Julie: Well, the funny thing is I never knew I was insulin resistant, no one ever told me that. But I was experiencing hypoglycemia on a regular basis. So I was having these ups and downs all day long. So as I cleaned up my diet, healed my gut, began to eat real food, and eventually ate a ketogenic diet. Plus I extended my fast for a long period of time, which got me into ketosis and exercised every day. The clarity was amazing. But I think what was even more amazing was that those ups and downs were gone. I had steady sense of energy all day long. So I think being in ketosis, however you do it, is critically important.

Dr. Bredesen: Yeah, so a couple more questions here. So let's see, Susan is saying, recommendations for fatigue? Did you have things Kat that you recommended for people or that you do typically recommend for your patients who have fatigue?

Dr. Kat Toups: Well, fatigue is a mixed bag, right? It's a symptom and it doesn't tell us what is causing that fatigue. So the first thing is to really do investigation, what is causing the fatigue? And so many things can cause that, but the kind of things that we address with the nutrients, the diet, as Julie was just mentioning, she got tremendous energy and stability from being in ketosis. So fat is a beautiful source of, it burns it into a clean energy, And you don't crash and burn like you do eating sugar. 'Cause when you eat sugar or carbs, you go up quickly with your blood sugar and then you crash really quickly, and then you're kind of up and down. So I think, just pretty much the things that we had people do as part of the protocol. And fatigue is so common in our society today, but none of my 10 patients, definitely none of them had problems with fatigue as their symptoms.

Dr. Bredesen: Isn't that interesting? And then what about Neuro-Lyme? And I know you had some of the people who had mycotoxins did you have any who had Lyme?

Dr. Kat Toups: Yes, I did have, I would say at least four patients that did have Lyme disease or babesia. I think some had Lyme and some had Lyme and babesia. And in my patients, there's Lyme, I talk about Lyme in little letters

and Lyme in capital letters. Some people have Lyme and they're very, very sick, and it's pretty obvious that something's going on. but in all of my patients that we turned up markers for Lyme and other coinfections, none of them were aware that they had it. And Lyme is such an interesting critter because some people it attacks their joints right away, and they know, they have either inflamed joints, they have infusions, but we know that Lyme is a spirochete just like syphilis, it likes to live in the brain. so it can live there and be causing symptoms over time, all of these infections in the brain. We're getting signals for more and more infections. I have a long list, more than one page long of infections that I've researched that can affect the brain. So when these infections are in our brain then they're triggering our immune system, which is designed to try to kill the invaders. Then that causes cascades of things like the amyloid production and destruction of the neurons. So I think it's very important to test for infections. And I think this is something that's being missed by a lot of people. And you can definitely start this protocol with great help from a health coach and a nutrition person. But I do think it's important for people to see a physician that can also test for a variety of infections. The herpes viruses, Epstein-Barr virus, which is a kind of herpes virus, are all things that we targeted in our protocol. But definitely we had people that did have markers for Lyme and that by the end of this study, we cleared it. One of my patients still had some markers and still needed some ongoing treatment after the nine months. But in combination with all the other immune support that we did, the Lyme in little letters, we were able to take care of during the study.

Dr. Bredesen: I think this is such a good point, because these spirochetes, as you indicated, live in our bodies without our recognizing it for years, and these other chronic infections like had Julie mentioned earlier, the babesiosis, not a spirochete, but that's absolutely a parasite. But same idea, it's a malaria cousin basically. So these various organisms, these chronic ones, have ways to live. And this is the neurosyphilis of the 21st century, just as people in the earlier centuries, 18th and 19th centuries, and even well into the 20th century, it was common to have neurosyphilis and it had go on for years and years until you had dementia, or you had a stroke, or you had so-called tabbies, all sorts of things that it gave you. And Lyme, we're not recognizing it enough. And it does live for many, many years and it's important to get rid of it and to

actually identify it and treat it. Suzanne asks, my mom used many supplements, she says they cause her kidneys, so it sounds like maybe some kidney effects, could you please help? So as far as what to do, first thing I would do, there's a wonderful little book which is called, "The Toxin Solution" from Dr. Joseph Pizzorno, I recommend it highly. And he talks specifically about kidney failure and the things to do and kidney failure related to various drugs and toxins and things like that. So clearly, if it's temporarily associated with specific supplements, of course, you want to get off those. And so now you want to kind of start from the beginning, start by getting off them, start to re-introduce and then please take a look at that book, it's really an excellent book. So, all right, so let's wrap up here on the trial.

Comparing This Trial to Others

Dr. Bredesen: Kat, let me just say again, congratulations. I know you differed as far as how many hours, but I know you spent hundreds and hundreds, if not thousands of hours preparing, seeing patients, getting them to do the right things, analyzing the data, keeping up with all the issues that arose, having your patients meet, worrying about it, checking everything, did we miss anything? Just incredible. And your patients showed tremendous improvements, as we talked about, two of them that started at 19, went to 30, the other one ended up at 29. I know definitely the pandemic set things back a little bit, despite the pandemic, which hurt other trials, came through with flying colors, statistically significant results. Very, very exciting. And again, Julie, you are living proof that this sort of thing, with your ApoE4 status, and your symptoms that you had years ago, responds so beautifully to doing the right things, to root cause analysis and to getting on it. And your babesiosis is proof that continue to tweak things is really, really important. So I recommend everyone please keep tweaking, please keep optimizing. And we'll definitely be in touch with everybody as we get this next trial going. Again, Kat, congratulations. Thanks for all the fantastic work, all of the great trials that you did and fantastic. Maybe just talk about, of all the trials you did, did you ever see positive results like this before?

Dr. Kat Toups: You were saying all the great trials, I was thinking, no, all the failed trials. I mean, every one of the trials I did, some of those drugs came to market like Aricept and Namenda, but the metric for coming to market was that the people on the drug did not decline as fast as was expected, but nobody got better. I did trials of things that didn't come to market, there was one that we could show on the PET scans was wiping out the amyloid plaques, but people didn't get better. It didn't translate into clinical improvement. And as you have so aptly described to people already, the amyloid plaques are protection right, because it's telling us the brain is being injured or insulted and that's protection. So taking away the protection might render the brain even more defenseless. So no, nothing worked. And I did finally, after so many trials, every new drug that I worked with, I would have hope, okay, this is going to help my patients that are suffering and they didn't work. So it's triply exciting, because, not only did people not decline faster, but a majority of them got better. And I believe our average improvement in the MoCA was a little over three, but that's the average. And as Dale mentioned, I had patients that started at a 19 that finished at a 30. So I had some patients that had really dramatic improvements. I was just looking at my numbers, and six of my patients are completely normal in their testing, there's no way they would qualify for any kind of study. Their MoCAs are 28 to 30. And the other cohort are kind of in the 24 to 25 range. And as Dale mentioned, even a few points change on a MoCA translates to huge improvements clinically. So just for me again, the hope that this should bring people, that it is worthwhile, there's no one size fits all. So the people that are struggling and they're not better yet, keep trying, maybe have a consult with somebody different that can look at everything with a fresh set of eyes, but you have to dig for all the factors. And I think, an important point that Dale's always made, about all the holes in the roof that have come to be so many holes now. We can't tell you how many there are, but you do have to kind of address everything. That just doing part of the picture, people who pick and choose what they do, they do not get the improvements as when we go full court press and people are really compliant and do everything. As Julie said, this is her lifestyle now, and it doesn't cause her angst. Look at her, she's beautiful, she's glowing, she's done amazing things. It's difficult in the beginning, trying to get all the pieces together. But once you hit that, and I could see my patients just improving. And even the amount of time they spent doing things, we had certain amount of minutes they had to do their HeartMath and have a certain amount of

minutes for their brain training, a certain amount of hours of fasting at night, I guess we didn't mention fasting, but intermittent fasting and time restricted feeding are important things for autophagy and other things that can help the brain. And I'm looking at my patients, how many hours, and they might've started fasting like eight or 10 hours and I could see them getting longer and longer and longer as they got used to it. So the more you work, I feel like that's one of the biggest markers of success and who gets better. And I don't mean to say that if you're doing everything and you're not getting better that there's anything wrong with you. It's just something, I feel like something is getting missed. Let's keep looking and looking and see what is being missed there. It does take a lot of investigation.

Dr. Bredesen: Yeah, absolutely. And even if you start small, you can add, work with with health coaches, get things all together. There's so much that can be done. But the bottom line, as always say is the armamentarium, which we've been told is zero, that there's nothing you can do for cognitive decline. It's the opposite, it's huge. There are so many, we just talked about it, a few things like the LDN and the diet and the HeartMath are just a few of the many, many things today. So there's a lot to do. Thanks to everyone for the excellent questions, Thanks so much to Kat and thanks so much to Julie and we look forward to seeing everybody next time.