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Clinical Nutrition Management of Cognitive Decline

Narrator:

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Dr. Bhatia:

You're listening to ReachMD, and I'm your host, Dr. Taz Bhatia. Joining me today is Dr. Dale Bredesen. He is Director of the Neurodegenerative Disease Research Center at the David Geffen School of Medicine at UCLA and Founding President of the Buck Institute for Research on Aging.

Welcome, and welcome to the program.

Dr. Bredesen:

Thank you, Taz.

Dr. Bhatia:

Dr. Bredesen, there is a new paradigm on Alzheimer's and cognitive impairment. You spent a lot of your life's work working on this particular condition. Tell us a little bit about how you see Alzheimer's differently maybe than what a lot of us were conventionally taught.

Dr. Bredesen:

We were taught that Alzheimer's disease is due to amyloid being produced in the brain and then ultimately tangles that are related to tau, and what our research suggests is something very different. It actually suggests that you make amyloid in response to metabolic and toxic perturbations, so essentially, this is a protective response. It is involved with downsizing of the neural network, but the reality is that when you look at the metabolic and toxic perturbations, they are what's driving the production of the amyloid. So, our research suggests that the idea of getting rid of the amyloid without understanding what's actually causing it to be there in the first place is a biologically naïve way to go.

Dr. Bhatia:

So that is fascinating. How does that impact for providers their clinical approach to a patient with Alzheimer's? It really sounds like they need to take a completely different approach rather than just thinking about removing amyloid.

Dr. Bredesen:

I think for the future, first of all, I think we will have much larger data sets, so we want to know the genome of the person, we want to know many different… we typically measure about 60 different metabolic parameters to understand, and when we do that, we can see, in fact, that there are subtypes of what is called Alzheimer's disease. And then we want to address those abnormalities which then alters the brain's response as opposed to trying to get rid of the response without addressing what's actually causing it.

Dr. Bhatia:

So, in taking this multidimensional approach, you mentioned gene sequencing or genomic identification. What do you think step 2 would be in trying to tackle this?

Dr. Bredesen:

So, step 2 is metabolic profiling. So we want to know everything from your hs-CRP to your copper/zinc ratio to your pregnenolone to your free T3 to your TSH, on and on and on, so that we have a look at what's actually driving this change that we ultimately call Alzheimer's disease.

Dr. Bhatia:

So, that's a completely different approach to Alzheimer's and what a lot of us have been taught. What clinical studies and observations have you done or have you carried out, and what kind of results have you seen?

Dr. Bredesen:

That's a very interesting question, because this all started back in 2011. We submitted a request to the IRBs in Australia, both the public and the private, to do the first comprehensive trial for people who had MCI, mild cognitive impairment, a pre-Alzheimer's condition, and what we were told is that it had too many variables. The problem, of course, is that Alzheimer's disease we realize is not a one variable disease, so we need to look at many of these different things. And going forward, this is exactly what we're trying to do, to put together a trial that will allow the entire symphony, the entire piece here, as opposed to just attacking one thing at a time. That's the idea. So what we have been doing until now then is working with practitioners who see patients and just simply bringing them up to speed on the latest research and on what are the critical parameters that are helpful to measure and how to go about looking at each of those parameters.

Dr. Bhatia:

Let's, maybe, spend a few minutes there, because I think it would be so helpful to the doctors seeing patients with cognitive impairment or Alzheimer's to really understand what the right approach to this, because any time you talk about a disease process as multidimensional, it gets a little bit overwhelming in a clinical setting. Where do I begin? Where do I start first? So, maybe walk us through that. Where is the starting point? Is it first measuring biomarkers, some of which you've already mentioned? What do you think the most important ones are? And then where would we move on from there?

Dr. Bredesen:

I think it's important to combine the imaging, of course, typically volumetric MRI with or without PET and with or without SPECT scans, with, of course, functional assessment. Where does the person stand on neuropsych testing, quantitative neuropsych testing? And, of course, you can do a lot of this online now, and there are also, obviously, neuropsychology experts who do this as well. Then with the genetics and the biomarkers, we believe that metabolism and exposure to various toxins are critical things to know. To be trying to treat this illness without knowing the metabolic status is a little bit like flying blind, so we believe that combining that set of things is helpful. And we actually have set up courses that will start later this year to teach practitioners which things to look at, what are the various

nuances of addressing this. We have some exciting results with people who have increases, for example, in hippocampal volume, dramatic improvements in neuropsych quantitative testing and things like that.

Dr. Bhatia:

And then some of the biomarkers you've already mentioned, testing CRPs; you mentioned pregnenolone. Anything else for the practitioner listening to us today that maybe they can't get to one of your courses; they're not sure really what else to test? Anything else that you would recommend?

Dr. Bredesen:

I'm happy to send out a list. There are about 60 different things that we test, so more than I can say in 30 seconds, but they do include many of the things that are associated with functional medicine, estimates of metabolic status.

Dr. Bhatia:

And you talk about Alzheimer's and cognitive impairment as this multidimensional disease, the amyloid being driven by all these different metabolic processes in the body. Let's break it down a little bit. What do you think you see most commonly in the world of nutrition and also maybe in the world of lifestyle and lifestyle medicine that the practitioner seeing patients day in and day out could go ahead and implement and put into practice when they're dealing with some of these patients?

Dr. Bredesen:

Well, let me start by saying that the body makes amyloids essentially for three different reasons, and again, as a protective response. It makes amyloids because it has been exposed to infection or undergone inflammation, and that leads to what we call type 1 Alzheimer's disease. The body also makes amyloids in response to trophic support withdrawal, so if you withdraw nerve growth factor, for example, or you withdraw estradiol, for example, then there is a response that includes amyloid as part of a downsizing. And then the third reason is you make amyloids also as toxin binders, so things like mercury, for example. Amyloid is very good at binding divalent metals, things like mercury and copper and things like that, and also things like other toxins, mycotoxins and things like that. So, those are three very different reasons -- and certainly, there can be mixtures -- those are three different reasons. And, for example, if you see someone who has one of the most common problems, which is insulin resistance, high hemoglobin A1c, high fasting blood sugar, that sort of thing, high fasting insulins, these people have what we call type 1.5 because they have both the inflammatory part of the type 1 and the trophic lack of support because of the insulin resistance. Insulin and IGF-1 are important trophic support for the brain, so you're having problems on both of those.

So, when you go through how to address these, you start by looking at what is actually driving the process and then go from there to it includes everything from key nutrition items. We want to know what your B12 is, what your vitamin D is, what your copper to zinc ratio is, what your free T3, free T4, all of the hormones as well; pregnenolone we talked about before, your estradiol to progesterone ratio; what is your testosterone status, all of those things. What is your cortisol status? Very high cortisols, of course, are very damaging to the hippocampus. And then, beyond that, we want to know nutritional things. We want to know sleep. Do you have sleep apnea? Sleep apnea is one of the most common missed things that contribute to cognitive decline. How much are you sleeping each night? What's the quality of sleep? What are you doing in terms of your sleep hygiene? All of these are critical. What is your stress level, of course, even things related to hygiene, your albumin to globulin ratio. Looking at this can actually change this metabolic profile. And what we find is, as the metabolism goes, so goes the cognition.

Dr. Bhatia:

And I'm curious too, taking this multidimensional approach -- and even in my practice we see a range of patients with a particular condition, so I'm sure people with severe cognitive impairment and then those that are milder -- is there a group of patients that won't benefit from taking this approach? Is it too late for some folks? I mean, kind of what do you think in terms of who benefits most from

nutrition, lifestyle modification, hormone evaluation, inflammation status? Who benefits the most from that? Is it just the patient with mild to moderate disease, or can even the most severe of our patients benefit as well?

Dr. Bredesen:

It's a great question. We don't know yet how late this will work. As with any of these others, the earlier you get it the better, and so we encourage people come in as early as possible; and, in fact, if you're at high risk, come in when you're presymptomatic. We say that the children of Alzheimer's patients are special people because they have a head start on prevention. They can come in early and get your profile checked out and see if you actually need to be on a program of prevention.

Clearly, after the presymptomatic phase, there is the SCI phase, subjective cognitive impairment, and that can go on for 10 years, so you have a long period where you can do a lot. After that is MCI, mild cognitive impairment, which often lasts several more years. Then you enter Alzheimer's when you actually change the ability to do your activities of daily living. Late Alzheimer's, this is probably not the best way to go, but there isn't anything right now that's particularly good for that either, so the earlier the better, but as we get toward the end, we want to know, well, what sorts of things do we need to add to improve even in later? And we have had a few e-mails from various people who have gone on the program late and have actually noticed improvements in their parents, in their siblings and that sort of thing.

Dr. Bhatia:

I mean, that is amazing and fascinating for the clinician who's seeing somebody. Now, if I'm seeing somebody and I'm trying to decide if they have subjective or mild or severe cognitive impairment, what are some things that I can very quickly latch on to? Should I be looking at age? Should I be looking at things like memory? For all of us out there practicing day-to-day, what are things we should be asking in the exam room to maybe assess whether this patient is somewhere in the spectrum of cognitive impairment and Alzheimer's so we can put into motion some of which you're talking about today? I know we have biomarkers that we've already discussed. That's helpful. But sometimes you don't even think to order the biomarkers unless you're thinking about the history. So, what things would you pull and really emphasize that physicians need to be asking?

Dr. Bredesen:

Well, there are some very simple tools to use starting with just asking the spouses because they often notice very early on, and asking the person themselves, “Have you noticed changes?” And I don’t call these people patients because these are often just either asymptomatic or just beginning symptoms. These people are just beginning to notice changes that many of us notice as we age. The second thing you can do is have a spouse fill out a form AQ21, which just looks at what complaints are there. And then there are many simple instruments, whether you use MOCA -- I like to use MOCA. It's a simple 30-point scoring system. You can do it in about 10 minutes, and I find that very helpful. Other people like to use MMSE, the mini-mental status. Some people like to use SAGE. That's an easy one to use, and people can use it at home with their partners. So there are many simple ways to get at who is having problems. By definition, when you're still scoring in the normal range but you know there are cognitive problems, be they memory, reading, speaking, spelling, math, things like that, when you are still scoring in the normal range, you are by definition SCI. It's subjective cognitive impairment. When you move to the point where you actually are testing abnormal on one of these tests or multiple of the tests, then, by definition, you have MCI, mild cognitive impairment. You know there's a problem. The test shows that there's a problem. But when you then move to where your activities of daily living are affected, that's, by definition, Alzheimer's disease.

Dr. Bhatia:

I see. Any last kind of final thoughts about key therapeutic things to consider or clinical things to be thinking of for our physicians listening today?

Dr. Bredesen:

I think the key point to drive home is that 21st Century medicine is taking over from 20th Century medicine. In 20th Century medicine we had small data sets. We said it's Alzheimer's disease, that's it, there's nothing we can do about it. With 21st Century medicine, there are many things to be done, there's a lot more to do, and there are larger data sets to be collected and then many things that we can address based on what we find in those data sets.

Dr. Bhatia:

Thank you for joining us today, Dr. Dale Bredesen. I know we've all learned a lot about cognitive impairment in Alzheimer's.

Narrator:

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