

Welcome to the Cutting Edge Health Podcast with Jane Rogers, where we discuss science to help prevent cognitive decline.

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[00:00:00] Jane Rogers: Welcome to the *Cutting Edge Health Preventing Cognitive Decline* podcast. I'm Jane Rogers. We're living in a whitewashed research world when it comes to Alzheimer's disease. It's White brains that have been studied and most participants in dementia research are not people of color. Dr. Lisa Barnes has worked for a quarter century to change that.

Educated at the University of Michigan and UC Davis, Dr. Barnes joined the faculty of Rush Medical College in Chicago in 1999. Since 2004, she's been the principal investigator for the Minority Aging Research Study in Chicago. It's one of the nation's largest brain studies focused only on Black Americans. Dr. Barnes, I would like to welcome you to the podcast. I'm so excited you're here. Thank you.

[00:00:47] Lisa Barnes: Thank you for having me.

[00:00:50] Jane: I've been a fan for quite a while. I read an article about you last spring that just so impressed me with the work that you have done in your career as a cognitive neuropsychologist. Walk me back. Tell me your story. How did you get involved in doing this?

[00:01:05] Lisa: Great question. I have always been interested in the brain from a very, very young age. I thought I wanted to go to medical school, however, to become a neurosurgeon or something fancy. After working in the hospital and just really working closely with the elements in the hospital, I realized that that wasn't for me, but I still wanted to study the brain.

I had a seminal event happen in college. I had an opportunity to have an internship with a very famous patient named H. M., and this patient actually is in all the textbooks. I'd read about him for many, many years. Just the possibility of working with him just never ever crossed my mind. I had an internship in Boston where he was being seen as a patient during the summers. Just to give you the background on H. M., he had intractable epilepsy from a very young age. It was just so disruptive to his life, 28, 29, 30 seizures a day.

[00:02:12] Jane: Oh, no.

[00:02:13] Lisa: He really could not function. They performed an experimental surgery on him where they removed a part of the brain that we now know is important for memory. It's called the hippocampus. They removed it on both sides—

[00:02:12] Jane: Oh, no.

[00:02:28] Lisa: —because that was where they determined was the site where the seizures were starting. This was a long time ago. We didn't know a lot about memory in the brain. They removed where they thought the seizures were occurring. It happened to be the seat of memory. He developed a profound amnesia where he could not remember new things, new facts, or anything.

We learned a lot about amnesia and memory from him. At that time, he was just in the textbook for me. You know how you go to college, you read all these famous stories. Just to be able to actually meet him and work with him during my internship was amazing and life-changing because it really solidified for me like, "Oh my God, this is what I want to do. I want to study memory."

Fast-forward, I did all the things that you're supposed to do to go on to school and get your degree. I always had my sights on understanding memory. I have all these different experiences where I've been able to work with rare patients who have different parts of their brain either lesioned or removed, so trying to understand, how that part of the brain was responsible for behavior? That's been my real interest.

Then after I finished my postdoc at UC Davis, I wanted to come back home to Chicago. I started looking for jobs. I saw this job where I am at now at Rush that was in Alzheimer's disease, which is also a disease of the brain and affects memory primarily. I was like, "Wow." I hadn't really studied Alzheimer's disease. I had really mostly been focused on these rare patients and stroke victims and things like that.

I said, "I'll give it a try." When I came here and I interviewed and I found out about the job, I was like, "Oh, wow, this is something great," because they were looking for someone to start a focused research program in health disparities to understand how this disease affects different populations. That was over 24 years ago. I've been here ever since. That's my story.

[00:04:40] Jane: Thank you for sharing that. Over those 24 years, you've done so much. You have written 300 research papers. People don't do that. This is huge.

[00:04:52] Lisa: Well, people do that, Jane.

[00:04:54] Jane: You think? Do you sleep?

[laughter]

[00:04:56] Lisa: It's a team science effort. I think that's one thing that really needs to be stated, is that in science, we work together. It's a collaborative effort. I'm not sitting at my

computer writing 300 papers. I'm working with people, different groups across the country, collecting these data, and then we're writing the results up. This is like a labor of love with thousands of co-investigators across the country.

[00:05:24] Jane: In these 24 years, you've started something very special. You realized there was a problem, that Black people were not being studied when it comes to Alzheimer's. What did you do about it? You've been very successful. Tell me about that project.

[00:05:39] Lisa: One of the things that we learned was that there was this real under-inclusion of Black participants in research. A long time ago, they were included for the wrong reasons. That's part of the reason why they're under-included now—because there's a lack of trust based on how they've been treated. Because Alzheimer's disease is a health disparity, it seems to affect certain populations more than others.

I knew that we needed to have more information on Black people. I went to the community with my team, and we started to just build relationships with people in the community and to really try to raise awareness about Alzheimer's disease and to raise awareness about the importance of research and what we were trying to discover. It took a couple of years just working in the community, building relationships, building trust.

Then when I got my first grant, I went back to the community and said, "Look, I got this grant. Would you like to be in the study?" and basically went around to different churches, and senior buildings, and clubs, and fraternities, sororities, anything that caters to older Black adults. I went there and gave a presentation either on healthy aging or risk factors for Alzheimer's disease, or whatever the community wanted to hear.

Then at the end of the presentation, we recruit for the study. We tell them about it. We invite them to be in. People think about it. Some people sign up right away, others go home and think about it. Over time, we have been able to get over 800 people in the study who we've been following since 2004. We're approaching 20 years of data on this population of people.

[00:07:20] Jane: Fabulous. It took, I was reading, a lot of convincing at the beginning. You've been into all of those 800 homes almost?

[00:07:29] Lisa: A lot. Maybe not 800. When I first started the grant, it was smaller, right? It was about 350 people. That was the target goal in the very beginning. Over time, the study has grown because people have heard about it, and they've told their friends. People are constantly enrolling. Now we're at 800. I could never visit 800 people. In the beginning, yes, that was important because I really wanted to thank people for believing in us and trusting Rush to be a partner with them.

Everything in our study is done in the person's home. We never have people come to Rush, to the hospital, right? We're trying to remove the barrier of transportation that many older adults have and also navigating a complicated medical system, right? We send our testers out to the person's home at their convenience, and they do the testing. Then we send a research assistant. We send a nurse. We send a phlebotomist to take blood. Then I would go as the last person on the list.

I was just going to go to thank them and answer questions. I was paying a 15-minute visit. It was never 15 minutes. People were so excited that "The doctor is coming to my house," and then they would see me, and they're like, "She looks like me." Well, I was like a granddaughter, right? That was many years ago.

[00:08:55] Jane: No, they'd still say that.

[00:08:56] Lisa: Maybe. I think that was like really important for the study, though, because it really showed people that we care about them, right? They're not just a data point. Because we're in their homes every year, we've developed this relationship with people. Even though I don't get to go into the homes now to have these conversations, I do put on these retention events where people come together, and we share what we've learned in the study. We answer questions.

Over time, I have had other investigators bring on studies, so I invite them in to describe what they're doing, what they're learning. It's really been like a feedback-type situation where we're learning, they're learning, and that's been really instrumental in keeping the study going for so long.

[00:09:45] Jane: I want to find out more about the study and what you're learning. First of all, tell me why the deep-seated reticence within Black Americans for participating in something like this, why did you have to overcome that hurdle first?

[00:09:57] Lisa: Yes, there are so many different reasons.

I think the one that people talk about the most is lack of trust in healthcare, in the medical establishment, and in research in particular because there has been a very sad history of exploitation and abuse when it comes to research with Black Americans, dating back years and years before I was even born. Black people were experimented on, like some of the famous studies are with the gynecology studies with Marion Sims, but there's just so many other areas where they have been experimented on.

There has been this sentiment that we're going to experiment on them. Oh, the Tuskegee Airmen, yes, that was huge. That's been a huge barrier because a lot of people in my cohort are at the age where they remember those things, right? Just trying to overcome

all of that, there's been a sentiment that "I don't want to be a guinea pig. I don't want to be experimented on."

Really being able to be transparent and explain to people why this is important, what we are looking at specifically, I think has been really good because, in a lot of those other studies, there wasn't really a lot of informed consent. People were enrolled without knowledge of what they were getting into, or they weren't given the results. What we try to do in our study is we give first before we ask anything and then we give back, right?

We're not just going to be a helicopter researcher: we come in when we have the grant money, and then they don't see us again. We're there. Whether or not we have the grant funding, we're in the community, and we are asking questions. We are asking them, "What do you want to know about? What's important for your brain health?" and then incorporating that into the study.

I think they feel like they have some ownership when we do that because we're asking questions that they care about. I think lack of trust is probably the biggest barrier that we've had to overcome. Then I think the other thing has just been a lack of awareness because before, if you looked on TV or the advertisements, you only saw White people. People thought Alzheimer's disease is a White person's disease, or they thought we're supposed to lose our memory when we get older. There's nothing you can do about it.

I think having to debunk some of those myths has also been a big part of the barriers that we had to overcome. I spent a lot of time just educating about what is Alzheimer's, what is healthy aging, and why, even though there's no cure, what are the things you can do to prevent or slow the onset of the disease.

[00:12:35] Jane: Now, now we get to talk about your studies. Tell me some of the significant things that you've learned.

[00:12:41] Lisa: We've learned a lot over the time we've been working with people. I think the things that I like to focus on the most are the social determinants that we are looking at because when people think about we're studying African-Americans, a racial group, they might automatically think that race is biology, that there's these biologic differences between Black people and other people, but that's not the case. Race is a social construct.

There are these social conditions in which people live that can affect our health. We have been looking at those social determinants to see how they might impact brain health. There have been a few that really stick out to me that speak to the context in which people live. One of them has just been discrimination. We have a very simple scale, a nine-item scale that asks questions about how often you experience unfair treatment, like going to a store or restaurant or being harassed or called names.

We found that people who report more experiences of discrimination, they perform more poorly on our cognitive function tests. They have more C-reactive protein measured in their blood, which is an inflammatory marker. We also can see that they have different functional connectivity in the brain because we also do MRI scans of our participants. The areas that seem to be affected are the same areas that are involved in trust perception.

There's some link there between being treated unfairly and distrust, this lack of trust. Then we were also trying to understand, "Could it also be related to the pathology that we see in the brain?" because what I didn't tell you is that another part of the study, which is unique, is that we are also recruiting for brain donation because Alzheimer's is a disease of the brain, and almost all of the studies have been just of White adults.

We have very little brain tissue from Black adults. A big component of our study is to try to get people to sign up for a brain donation and then we try to get their brain when they die. We're trying to understand: are the experiences of discrimination associated with any of the pathologies that we measure in the brain at death? We're starting to see a signal of that.

[00:14:57] Jane: That cohort experienced so much discrimination. You wonder if past discrimination, not just what happened yesterday, but what happened 40 years ago, 50 years ago, how does that affect the brain?

[00:15:08] Lisa: That's a great, great question. It's just a little hard to study that because you have to rely on recall, right, because it happened a long, long time ago, and these are older adults. We have tried to get at that indirectly. In one study, we asked people where were they born and where were they living at age 12? Everyone lives in Chicago now, but about 40% of people migrated here from the South.

These are people who were born in the '20s and '30s. It was during the Jim Crow South era. We asked them where were they born? We asked them had they ever attended a legally segregated school? Because this is the first generation of people to attend legally desegregated schools because, before the Brown versus Board of Education ruling in 1954, schools were segregated by race.

We asked that question, and we tried to see if that was related to brain health. We found a very interesting result. We found that people who were going to school in the South and reported attending a legally desegregated school had worse brain health in old age than even their Southern counterparts who were going to a segregated school. That was surprising because we thought the segregated schools would be worse because poor quality, fewer resources, but it was actually going to school with other White children that was negative for them.

We're not saying that desegregation is bad, but think about the time, right? In the 1950s or right after 1954, you're going to school with people who don't want you there. The teachers don't want you. The students don't want you. The parents don't want you. These are children, right? You've seen the pictures. You've seen people being escorted, with the security people, so it was a really toxic climate during that time.

We think that that early life experience probably had an impact on people. It was a stressful time, right? We can see it 50 years later when we're measuring their cognition that they are performing more poorly. That was really striking to us. It was an indirect measure of early-life discrimination. Other studies have shown this early-life trauma. Think about the Holocaust. It has an impact on people that you can measure decades later.

We're trying to understand things like [early life discrimination] to understand the context in which people are living to help us understand what we can change. Maybe it's policy, maybe it's social structures to help people age better.

[00:17:51] Jane: One of the things that you found, I understand, is that APOE4 is different in Black patients than White patients. Is that right? Because then that's known as the Alzheimer's gene, but it doesn't react the same way.

[00:18:05] Lisa: Right. That's what's one of the things, is one of the most robust genetic markers for Alzheimer's. That seems to be the case in White people. This gene actually carries cholesterol, right? You get one from your mother and one from your father. There are three different isoforms. There's the E2, the E3, and the E4. The E3 is neutral, and it's most prevalent in people. E2 is protective and very, very rare. The E4 is the risk allele.

That's the one that's been shown in numerous studies to be associated with Alzheimer's. Not just our studies but studies across the country have shown that Black people don't have the same risk, even though they have the E4 gene. In one of our studies, what we did, we looked at a neighboring gene called TOMM40. It's just right next to the E4 gene. In White people, those two genes are on top of each other. It's called disequilibrium in White people.

Since all genetic studies have only included White people, it was thought that the TOMM40 gene was doing nothing other than what the E4 was doing. They're doing the same thing, right? We have a study with Black people. When we looked at the pattern of TOMM40 and E4, we saw a difference. We saw that some Black people had the same pattern as Whites, but others had a different pattern.

It was the people who had this different pattern who were showing a decreased risk in decline or decreased risk in Alzheimer's. What we think is going on, if you think about Black people in America, they came from Africa, right, through the slave trade, and there's

been a lot of admixture, a lot of mixing of the races. Some people have a pattern that looks very European, and some people have a pattern that looks very African.

What we think is that admixture is diluting the E4 effect or making it look like Black people don't have a risk for E4. I think there's a lot more to be learned, but the thing that we learned about that study in particular is that if you don't have the data, you can't see these differences, right? We just thought for many years that "Oh, TOMM40 is not doing anything." If you have people of different races in your study, you can see that there might be different patterns of genes and how they're distributed, and that might help us understand a little bit more about the disease.

[00:20:32] Jane: I've also read that you think that Alzheimer's is not more prevalent within the Black community. Some people think it is, it's like twice as high in the Black community, but you're not sure about that.

[00:20:42] Lisa: I feel like we don't have enough data to say that for sure, right, because the data that we have does suggest that the risk is about two times higher. There are some issues because a lot of those studies use cognitive testing to make the diagnosis, and we know that Black people perform more poorly on those tests because they have fewer years of education or they have less quality education, right?

A lot of the studies are just a one-time measurement, not following people over time. When we follow people over time, we don't see any faster rate of decline in Black people than White people. You would expect to see a faster rate of decline if there's more Alzheimer's. I think more importantly than that, when we look at the brains, the pathology in the brain, we don't see any differences in the underlying pathology that causes Alzheimer's.

Because we don't have very many studies that have brain tissue, we are really relying on cognitive testing and other things that we can measure while people are living, right? I think now that the plasma biomarkers are out where we can measure some of these pathologic markers in blood, I think there's going to be a lot more data coming out, and we're going to get more information about how this disease plays out across race and ethnicity.

I'm not saying that it's not true; I'm just saying that we need more data, that I'm not 100% convinced based on what I've seen in the brain that the disease is more prevalent.

[00:22:18] Jane: More prevalent. Tell me about those plasma markers you're using.

[00:22:21] Lisa: We haven't gotten them back. We sent our plasmas out to be measured, but there have been a few studies. You can measure amyloid and tau in the blood now, which are the main markers of Alzheimer's disease, but you also can measure something

called neurofilament light, which measures just a general marker of neurodegeneration. There have been some studies trying to correlate the biomarkers in the blood with what you see in CSF or in PET imaging, and there's a very good correlation.

It suggests that what we're seeing in the blood reflects what's going on in the brain, right? There's a lot of hope that because that's a less invasive way to see what's going on in the brain, we'll be able to use that data to really understand racial differences. So far, I can tell you that there's been a few studies that have looked at the plasma biomarkers in Black people, and they are finding that there are lower levels of amyloid measured in the blood, which is one of the markers.

There's a small caveat with those studies. They've all been clinic-based studies, and we know that people who show up to a clinic are different than people in the community. We really need data from people who come from the community, and that's what our studies are doing, right? We don't recruit from a hospital, people who have medical care; we recruit directly from the community, and people don't have dementia when they start in my study, so we'll get a better sense of how these biomarkers develop and how they change over time in community-based participants.

[00:23:52] Jane: I think it's going to be fascinating, and you probably think about this, too. If you have 800 participants now in a cohort that's, what, 60s, 70s, 80s probably, as you get younger and younger participants, as people who are now 30 get to be 60, the education level is so much better. Discrimination is less. Are we going to see a decline in Alzheimer's in that population?

[00:24:19] Lisa: Oh, that's a great question. Very optimistic.

[00:24:23] Jane: I'd like to think times are changing.

[00:24:25] Lisa: I know, right? I would hope so. I just think that we're just really touching the surface of the social conditions that differ between people. There are so many-- Neighborhood effects are different, right? I think we're going to have to really change society at a global level to really start to see changes in Alzheimer's because it's not just individual treatment or what you get in school; it's your living environment. It's your access to healthy foods.

It's how you're able to get out and be physically active, and there are all these barriers to people being able to do that safely, based on how society has marginalized certain communities, right? I think we're going to have to change a lot about society before we can really start to see a decline in the disease if it really is caused by these social determinants, which a lot of data suggests that it is. It plays a big role anyway.

[00:25:25] Jane: Tell me about your dreams. You started as a Black cognitive neuropsychologist. You or probably a handful of other women who are in this field, have you mentored other women? Do you see the field changing? How have you quietly tried to change the field over your tenure?

[00:25:47] Lisa: Yes, that's a great question. I have mentored a lot of people, not just women, men, too. What I've really tried to focus on in my time, in the little time I have left in this world, is to really foster the next generation of researchers who are interested in health disparities and health equity. I just became a multi-PI of a coordinating center for the RICMARs. The RICMARs are Resource Centers for Minority Aging Research that are funded by the National Institute on Aging.

These are centers that their main focus is mentoring the next generation to do research, not just in health disparities, but in aging in general, to understand our aging population. I am now a multi-PI of the coordinating center for 18 different RICMARs. That is my dream, to be able to have a role to play in making sure that the next generation has the tools that they need to be able to really study health equity and really change the systems we've been talking about because it may not change for me, right?

These young people who are coming up now, they have such great ideas. They have so much innovation, so much creativity. They're going to change the face of Alzheimer's and how it's studied. I just want to be able to help the next generation. That's a big dream for me so that my children don't have to ever even think about Alzheimer's. It's just a distant "Remember that disease that used to affect people? That's gone." I want that to happen.

[00:27:28] Jane: That's going to happen. It will. Yes. Now, when you say multi-PI, that means Multiple Principal Investigator?

[00:27:34] Lisa: Yes. Sorry. Yes.

[00:27:35] Jane: No, I thought that's what it was.

[00:27:37] Lisa: Right. There are four of us in the Gerontological Society of America. They are the contact principal investigator. It's just a wonderful organization of researchers and policymakers. We get together once a year. Actually, our conference is next week in Tampa, to just display different research, caregiving research, basic science, social science, healthcare, the whole gamut is all focused on aging. They're one of the multiple principal investigators.

[00:28:10] Jane: Anything else before we wrap up that you want to communicate about your research, about the future?

[00:28:17] Lisa: Yes. I think the thing that I just try to emphasize when I go out to the community is that Alzheimer's disease is something that we can definitely conquer, but we need people. We need people to be advocates. If you're not old enough to be in a research study but you know you have a parent or you know someone who is old enough, let's take off the blinders. Let's just encourage people to become involved with research because all the new treatments that are happening right now and things are changing very quickly—

[00:28:53] Jane: Very fast.

[00:28:54] Lisa: —this is not going to work for everyone if everyone's not at the table, right? I want everyone to have an opportunity to be helped by treatments if it's possible, but we need people to be in the studies to even be able to say that this treatment works for you. I think the most important message I would give is: Let's raise awareness. Let's de-stigmatize this disease. Let's talk about it, and let's do something about it by becoming involved.

[00:29:21] Jane: Great message. Lisa, I just want to thank you for your time.

[00:29:25] Lisa: Thank you so much for having me, Jane.

[00:29:27] Jane: It's just been delightful talking with you. I hope you have a fabulous day and a deep bow to you for what you have committed your life to doing. It's really critical and important work.

[00:29:36] Lisa: Thank you so much.

[00:29:38] Jane: Very important. [music] You've been listening to the *Cutting Edge Health: Preventing Cognitive Decline* podcast. Any information shared here is for educational purposes only. Guest opinions are their own. This podcast is not responsible for the veracity of their statements. Do not use any of this information without first talking to your doctor. Cutting Edge Health LLC is not responsible for what may happen to you if you use their information in place of official advice from a medical professional. Thanks for listening. Be well.

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