Zoom In on **Dementia & Alzheimer's**

Frontotemporal Dementia: Diagnosis, Trials & Treatment
Thursday, September 26, 2024 | 1 p.m. EDT
Transcript of Zoom with Brad Dickerson, MD
Director, Frontotemporal Disorders Unit, Massachusetts General Hospital

BROOKS KENNY: Welcome to Zoom In On Dementia & Alzheimer's, brought to you by BrightFocus Foundation and AFTD. It's wonderful to be with you. I'm Brooks Kenny. I'm an Alzheimer's advocate and I'm an advisor to the BrightFocus Foundation. I sometimes have the opportunity to moderate these discussions. I've had Alzheimer's in my life with my mother-in-law, whom we cared for many years. And so I have personal experience. And really, I'm so inspired by the advocacy and research that's happening in the field.

BrightFocus Foundation, for those of you new to the organization, it is a nonprofit organization that has invested nearly $300 million in research grants, catalyzing scientific breakthroughs in Alzheimer's disease, glaucoma, and macular degeneration. And today's program is part of a series. We have a series called Zoom In on Dementia & Alzheimer's. And obviously, the title of this one is Frontotemporal Dementia Diagnosis, Trials, and Treatment. And today's episode is very special. It's supported by educational funding from Sano Genetics. And throughout the year, additional funding support comes from Biogen, Lilly and Genentech.

And the timing of this topic is certainly very, very exciting. This week, advocacy is happening all over the world on behalf of this topic. It's actually World FTD Awareness Week, which is organized by the Association of Frontotemporal Degeneration, or AFTD And the campaign really aims to shed light on this often misunderstood and misdiagnosed disorder. We are thrilled to be collaborating today with AFTD on this special episode. Dr. Shana Dodge, AFTD Director of Research and Engagement, is on the call with us and she can answer questions that you might have about resources. So if you have additional questions and you want to add them in the chat, you are more than welcome to do so.

We have a fantastic expert today. Many of you submitted questions in advance of this discussion today. Some of them were related to the topic of AFTD, and then others were related to neurodegenerative diseases in general. So I just wanted to call your attention to our list of previous episodes. They're here for you to see. If you go to Brightfocus.org/ZoomIn, you in can actually access those questions and topics rather and get more of your questions answered. And don't forget, we want to hear from you. So if there are topics that you're thinking about that are related to the work that we do, please put them in the chat. Please send us an email. We really do want to hear from you because we build these episodes based on the feedback that we get from our community. Lastly, I want to remind folks that when you are asking questions, we cannot answer anything personal, so please keep things general in nature. We can't provide specific treatment advice.

OK. Moving on, I'm actually delighted to introduce you to today's expert speaker, Dr. Brad Dickerson, and I'm going to warn my audience in advance that I'm using my notes because his bio has a lot of big words in it. And I want to make sure I don't leave anything out. He is a behavioral neurologist and neuroscientist dedicated to the sophisticated, compassionate, and multidisciplinary care of patients with neurodegenerative disorders, including Primary Progressive Aphasia or PPA, Alzheimer's disease, frontotemporal dementia, posterior cortical atrophy, and related disorders. He is the Tommy Rickels endowed chair of Progressive Aphasia Research, director of the MGH Frontotemporal Disorders Unit, the leader of the Neuroimaging Core of the MGH Alzheimer's Disease Research Center, and is a professor of neurology at

Harvard Medical School. He runs a multidisciplinary team of 30 clinicians and scientists using advanced brain imaging and behavioral methods to study how memory, language, emotion, and social behaviors change in normal aging and in patients with disease. His team also studies new approaches to caregiving. Dr. Dickerson, welcome to the program and thank you for all that you do.

DR. BRAD DICKERSON: Thank you. Brooks. It's a pleasure to be here with everyone.

BROOKS KENNY: So we're going to kick things off, again, with the questions that really came from this community. So many from AFTD are joining us today, so many in the BrightFocus community. But we want to just start with the fundamentals because I know there's a lot of confusion and we actually got a bulk of our questions related to what actually is FTD and how does it differ or how is it similar to diseases like Alzheimer's? If you could just start with the basics.

DR. BRAD DICKERSON: Sure. Well, I think if we think about a condition like congestive heart failure, we know that people can have symptoms that lead their heart to not pump properly. And that can be caused by a whole host of specific conditions that cause the functioning of the heart to not work right. Similarly with the liver, if someone has a diagnosis of cirrhosis, there are a variety of disease processes that may have led to that. With dementia, it's really a form of what you might think of as failure of certain parts of the brain to work right, and it leads to eventual loss of cognitive or behavioral abilities that allow people to function independently in their day-to-day life. But there are lots of causes of it. The most common is Alzheimer's disease. And the way we think about it nowadays is that's a very specific brain disease. It's not synonymous with all dementias. It just happens to be the most common cause in the brain. And it's made up of amyloid plaques and tau tangles that affect certain parts of the brain and lead to symptoms, most often memory loss, but often other symptoms as well.

And so with FTD, it's a different disease process that affects mostly the frontal lobes or the front part of the temporal lobes or both. And it's either got tau pathology, so this protein called T-A-U, tau. And these

proteins have normal functions in the brain, but what basically happens is they rust and twist and tangle and clog up the machinery of the cell and cause it to have trouble working. And so tau pathology can be found in one major type of FTD, and that's similar to but not exactly the same thing as the tau pathology that's in Alzheimer's. So there may be some overlaps there and treatments may help both conditions. With FTD, you don't have amyloid plaques. So that's the reason why the currently newly approved drugs for Alzheimer's, which target the amyloid plaques, are not something that's going to help people with FTD because there are no amyloid plaques in the brain.

The other major type of FTD, and we talk about it as frontotemporal lobar degeneration, which is meant to connotate the disease process in the brain, is caused by a protein called TDP-43, and that protein is also abnormal in people with ALS. Again, it's in slightly different forms of abnormality, a different part of the brain. But we hope that research on ALS will help with that type of FTD, and vice versa. So really, these diseases are related to each other in certain complicated ways, but they're separable and probably will need to be targeted by different types of treatments.

The other way that FTD is different from Alzheimer's is for reasons we don't understand, it tends to occur at a younger age, often in people's 50s or 60s. Sometimes could be older, sometimes can be younger. Tends to be a younger onset condition, not always. And it tends to primarily, at the beginning stages of the disease, not affect memory so much in most people, but rather language or personality and behavior, in especially social situations. So that's often not something that's recognized as being a neurologic problem. It's often thought to be, well, I should see a psychiatrist if I've got changes in my emotional or social behavior. And so that can lead to delays in diagnosis. Whereas if a person has trouble speaking, they're often referred to a neurologist for the question of could they have had a stroke or something similar. And it turns out they have a progressive condition that leads to loss of communication abilities, and that's the language or aphasia form of FTD.

And there are a couple of other forms of FTD that more often strike

the motor parts of the brain. And those are very alphabet soup names that include progressive supranuclear palsy, which unfortunately Linda Ronstadt is living with, corticobasal degeneration, and the condition that's FTD-ALS. So some people get actually both symptoms of FTD and ALS. So those three are really considered to be often the motor or movement-related forms of FTD. So that's one of the challenges, is that it's a different but related disease process in the brain and there are multiple different types of it in terms of the way people are affected in their symptoms. So it makes it really tough to recognize, even by sophisticated professionals.

BROOKS KENNY: Wow. Thank you. That was really helpful and understandable. I appreciate you breaking that down. And I think it really leads us to the next grouping of questions. Diagnosing neurodegenerative diseases is complex. I can say that as a layperson. I mean, I remember when my mother-in-law was diagnosed, it was a very confusing process and we had different diagnoses at different times. Can you help our participants understand how it often is diagnosed? I mean, it sounds like early diagnosis is not happening very often, but what are the tests that get done? And what's that diagnostic journey like?

DR. BRAD DICKERSON: Yeah, unfortunately, it's often a longer diagnostic journey than anyone would want it to be. And some of that is because it's often hard to access specialists that really know these conditions because many neurologists, for example, or neuropsychologists or geriatric psychiatrists might have seen a handful of patients with FTD in their careers and are not really specialists. So that makes it challenging because they're actually specialists, but they're not specialists in this particular set of diseases. So it makes it tricky. But anyway, what is typically done is the clinician will ask the patient and also someone who knows the patient well to describe what's been going on in their life, what kinds of symptoms are they experiencing. So that's taking a good quality history. The challenge there is that patients may or may not have insight into their symptoms. When people have the most common type of FTD, which is called the behavioral variant, they often don't realize anything's wrong. They may be behaving quite abnormally compared to how they used to be in terms of their emotional and social behavior, their personality, but not realize it at all. They may be making terrible decisions, may be losing money to scams,

may be basically committing crimes that are not thought to them as being crimes, but are viewed that way by society. So it can be very difficult because if you sit with the patient and try to get a history from them, they may not tell you anything's wrong. They may be frankly argumentative and deny that something's wrong. So you really have to try to get a history separately in that situation from the patient and from either the spouse or a child or a close friend or someone who knows the person well and who knows what they used to be like before the symptoms came on. And that's particularly challenging in some forms of FTD.

And then we do an examination, typically in person in the office. Some of this can be done by telehealth, which we've gotten better at since the pandemic, but some of it needs to be done in person. And so that's basically a cognitive examination where we talk to people about how they're experiencing symptoms in their life, if they have insight into them. And then we test them with various tests often starting with something simple like the MoCA, Montreal Cognitive Assessment, which is really a screen. It's not meant to be an in-depth assessment, but it's a starting point.

And then we typically do a psychiatric interview. We try to find out maybe the person actually has depression or bipolar illness which can come on later in life, even though that's unusual. And so interviewing the person about their mood and whether they're experiencing any kind of hallucinations or delusions is important. So that's the psychiatric interview.

And then the neurologic exam, which is trying to figure out, does the person have abnormalities in the movement of their hands, their walking, their eye movements, or other things that can be detected by a neurologist when they do an examination? Once we have all that information, then we usually have the beginnings of a formulation of what we should do next. Sometimes that is to get a full neuropsychological assessment by a neuropsychologist to really cover several hours worth of testing of thinking abilities and sometimes questionnaires about symptoms that the patient fills out and that someone who knows them well fills out.

And then we start to think about the actual medical tests. And we always want to get an image of the brain. So that's typically an MRI scan of

the brain, which tells us about the structure of the brain and whether there are any abnormalities of the structure of the brain. And we often end up getting a PET scan that measures the functioning of the brain, which for anyone who's a Medicare beneficiary, that's been approved for this purpose for more than 20 years now. Unfortunately, many private insurance payers are a little less forthcoming when it comes to paying for that. And so sometimes we have to do prior authorization discussions to get that test, which is a measure of brain function, that particular glucose PET scan. There are different types of PET scans. That's the kind of first line test that tells you if there's a problem with the functioning of the frontal lobes or the temporal lobes. There are not yet specific molecular biomarker tests for FTD, which is something we're working very hard on. That's really moved the field of Alzheimer's disease forward quite rapidly, which is to be able to get spinal fluid or do specialized PET scans to measure the amyloid plaques or the tau tangles in people with Alzheimer's disease. We don't yet have that for FTD, but we are getting closer to having those kinds of tests, which we really need badly.

So that's kind of the starting point for a lot of this. If it's not clear that a person has something within this family, they may have other kinds of tests, like brainwave tests, like EEG, or tests of spinal fluid to look for inflammatory or infectious conditions. So there's often a broader search for what might be causing the person's problems. But those are the general types of tools that we tend to use.

BROOKS KENNY: And so when I listen to that comprehensive kind of end-to-end diagnostic journey, it sounds very similar to what you would do if you were potentially concerned about Alzheimer's disease. And so is it ultimately when you get to the MRI or the PET scan where you can decipher whether it's-- I mean, symptoms sound a little bit different, too, but you ultimately need the images of the brain in order to understand the type. Is that accurate?

DR. BRAD DICKERSON: Yes. I mean, I think when people follow the textbook examples, which many people don't, but if a person is a textbook case, if you will, a lot of times a good clinician that is knowledgeable about these conditions, after just meeting with the person the first time

and doing the initial evaluation of the history and the examination, they may say this is very likely to be the semantic variant of primary progressive aphasia, a very specific form of FTD, or one of the other specific forms of FTD. And they may say, I predict that I'm going to see x, y and z abnormalities on the MRI, a, b, and c abnormalities on the FTD PET if it's needed. And then when those come back correct, it's essentially 95%+ accurate even if we don't have molecular biomarkers for FTD. But yeah, the general approach is similar across these different conditions, including Lewy body disease or vascular dementia. We're just about to publish some new American clinical practice guidelines for how to approach the diagnosis of these types of conditions. And it's really similar across the board, even though some of the specifics may vary.

BROOKS KENNY: Got it. And one question that we had that came in advance is someone with primary progressive aphasia diagnosis with Alzheimer's etiology. Is that another thing, another topic within the umbrella?

DR. BRAD DICKERSON: Yeah. So the way we like to think about what we call the diagnostic formulation-- so when you're a doctor or another medical professional and you're formulating a diagnosis, you might say this person has congestive heart failure. It's stage 1 because it's not affecting them very much at the moment, and it's likely caused by coronary artery disease with multiple heart attacks that have weakened the muscle. So that's really telling you what's the overall set of symptoms that a person is having, how severe are they, and what's the cause. We think the same approach should be applied to these conditions.

So the first question is, what's the person's cognitive functional status? And what I mean by that is, are they unimpaired? Are they without any impairment, but maybe subjectively concerned but you can't see any evidence that they actually have real cognitive impairment or losses of functional independence in daily life? Or do they have mild cognitive impairment where they may have symptoms, they may have evidence on testing that they have a memory or other problem? Language is a common example, which would be aphasia, but they're still functioning independently in daily life. They don't need someone to take over for their bill paying or their driving or their other high-level activities of daily living. Or they may have mild dementia, which means they have the symptoms

that we're talking about, whichever type they are, that's detectable on testing. And they've lost some degree of independent functioning as a result. So it may be mild, but they no longer are able to do their job anymore, for example, because of this condition. So that's cognitive functional status, which tells you essentially how independent or not independent are they as a result of this problem.

And then we get into syndrome. What's the syndrome? So primary progressive aphasia is a complicated name for a syndrome, which is where there's a communication problem or a language problem. It's the main issue, it's primary. And it's getting gradually worse, it's progressive. So it's really a descriptive term for gradually progressive communication difficulty in the absence of much of anything else.

And then the third thing is, what's the cause in the brain? Which of these diseases is causing it? We know that primary progressive aphasia can be caused by frontotemporal degeneration in the brain. There are two major types. Or it can be caused by an atypical form of Alzheimer's disease in the brain. It's one of the so-called atypical forms of Alzheimer's. And the characteristics of a person's language impairment are different usually between whether it's caused by Alzheimer's or whether it's caused by FTD. And usually, experts can tell the difference before they start doing all the medical testing. So there are forms of primary progressive aphasia that can be caused by Alzheimer's disease or by FTD. And generally speaking, there's a probability that that may be true for the other syndromes as well. So, for example, the behavioral variant FTD syndrome, which a lot of people think of as the classic syndrome, where the person is not how they used to be, personality and behavior-wise, usually is caused by FTD but rarely can be caused by an atypical frontal lobe predominant form of Alzheimer's disease or other conditions as well. So there are probabilistic relationships between the person's symptoms and their underlying changes in their brain. It's not one to one. That's one of the things that makes it really tricky.

BROOKS KENNY: Yeah, it's certainly complex. And building on that, we had a lot of questions about signs and symptoms. And I know you've talked about them, but. But generally speaking, what is the progression

of symptoms for FTD? When does memory come into play? And what-- we have two questions here I'm reading about what can we do if we think our loved one has FTD? So if you could talk a little bit about that. I mean, I know in the Alzheimer's-specific community, we spend so much time talking about early, early, early, and get a baseline, make sure you understand how your brain is functioning so that when things start to shift, you can get a hold of it much earlier. But I think this feels even more tricky given the behavioral symptoms. And I'm not sure how well-known this really is, that it's more the behavioral and communication. So if you could just speak a little bit to the community out there listening how to help a loved one if you suspect something is off or not right, and then what are some of the symptoms as someone progresses along the disease?

DR. BRAD DICKERSON: Yeah, it's a really challenging problem because typically, a spouse or a child or a close friend will be noticing symptoms, and the person with the symptoms may or may not also be concerned about the changes. A lot of times people with progressive aphasia are quite concerned about the changes. They may even be aware of them before their family members are. So there's a broad spectrum of the awareness and insight and distress by the patient. And when there is not awareness and insight by the patient, then it's up to the family member to try to figure out, how do I bring this to the attention of the primary care doctor and get a referral to a specialist? Because a lot of times, spouses or other people are often not allowed in the primary care doctor's office and may be actively discouraged from voicing their concerns. So that can be a very challenging situation to navigate. And sometimes people end up having to send messages through office staff to get to the doctor and make it be something that's on their radar. So ultimately, I think if someone is concerned that a person has Alzheimer's, a lot of primary care physicians feel comfortable doing the initial evaluation of that. If a person is concerned that their 50 or 60-year-old spouse or parent is beginning to have communication problems or personality changes, I think the most important thing is to try to make sure that the primary care physician is aware that there is a perception by someone who knows the person well of a problem. And then a referral can be made because most primary care physicians don't feel comfortable evaluating a patient for possible FTD.

Typically, the family members do research online and they read about the symptoms and say, oh my god, this might be what's going on. How do I get it evaluated? And so typically, the primary care doctor would refer the patient to a neurologist, a geriatric psychiatrist, or a neuropsychologist, and that would be the first line assessment. And it's always important once that is initiated, once that process gets initiated for the person who is the family member with concern to accompany the person to the visit, because it's so critical that that perspective be voiced, which again, I recognize is quite difficult at the beginning stages. But most of the specialists will encourage people to come with a so-called partner in their care to provide an independent perspective on what's going on in their daily life.

BROOKS KENNY: Absolutely. Yeah, it's so important. And I think it's why these conversations every month are critical because I think we need to try to break down stigma and initiate these conversations as often as we can with our friends and family and in our community. So really appreciate that. We have a lot of questions coming in on the chat, but I do want to ask you two more categories and then we'll turn to the chat. Never an easy topic, but we did have people, several ask what the end-of-life usually looks like and what is the typical cause of death when someone is progressing with FTD? So if you could speak to that.

DR. BRAD DICKERSON: Yeah, I think the different types of FTD are really separable at the beginning. Usually in the first few years, maybe three or four years, they start to merge then. So people with aphasia typically start to have trouble with memory. Almost everybody, sooner or later begins to have trouble with executive functions, which are their ability to make decisions and get things done. And people with the behavioral variant will commonly have memory problems. They'll almost always have executive function problems. They're often making poor decisions early on in the course of their illness. As it progresses, they'll often develop language and communication problems as well. Many patients will develop motor symptoms, difficulty walking, difficulty moving. Not as commonly difficulty swallowing, although the FTD-ALS type of the condition is commonly associated with that problem. And so the subtype that we

identify at the beginning is often very helpful at predicting what symptoms do we need to worry about going forward, and what may we need not to worry as much about, and what's the timeline for those symptoms.

So when people have FTD-ALS, meaning they have some form of cognitive or behavioral impairment that's typical of FTD, and they have motor neuron disease, meaning weakness in their limbs or in their swallowing and talking muscles, their survival is often quite short. Usually on the order of two to five years if it's that type, that's the most aggressive form. Whereas if people have some of the progressive aphasia forms, their survival can be a decade or sometimes longer. We've had people go for up to 20 years even. Because some of the patients don't have much in the way of motor impairments. So they don't end up bed-bound. They don't end up having trouble swallowing. And those are some of the risk factors for the end-of-life problems that are common to people with pretty much any kind of dementia. Once a person with dementia loses enough ability that they're basically not able to take care of their basic activities of daily living, they forget, in so many words, how to walk, how to talk, how to eat, and need people to help them with those things, they end up in a debilitated state that makes them vulnerable to opportunistic problems like infections, like urinary tract infections, aspiration pneumonia, bedsores, and the like. And those are often the end stage problems that are essentially complications of the disease that was there to begin with that lead to death.

And the range is wide. The average tends to be 7 to 12 years or so. I usually tell people somewhere on the order of not quite or around a decade. And again, it depends very much on how early it's diagnosed. Sometimes the diagnostic process takes long enough that people are already farther along when they get a clear diagnosis. And then obviously, there's less time. But most of the time when I hear that a doctor has told a patient, you've got one to two years to live, that's actually not true unless they have one of these rare, very aggressive forms. So I think a lot of less-experienced doctors think these conditions are actually more aggressive than they are. One of the challenges, too, is because they often affect young people, if the person is otherwise medically quite healthy, they might live for quite a while in a fairly debilitated state because their bodies are otherwise less vulnerable. So that can be another challenge of FTD that you don't see as often in Alzheimer's disease.

BROOKS KENNY: Wow. So interesting. Well, let's shift our conversation to genetics. And we have a question, are there any known genetic commonalities as it relates to FTD? What are the genetic propensities? And is genetic testing available? So if you could address the topic of genetics and some of those questions. A few other folks say they have a family history, can I get a genetic test knowing that there's already some for Alzheimer's?

DR. BRAD DICKERSON: Right, so like most of these conditions with rare exceptions, the vast majority of cases of FTD are what we call sporadic, meaning they don't seem to be associated with any known abnormalities of genes. But somewhere on the order of 15% to 20%, and these are estimates, we don't know the exact numbers, but I usually say around 15% to 20%, may be due to one of these single gene abnormalities that is inherited from parent to child with a 50/50 chance. And so these are not linked to the sex chromosomes, so they're equally possible in males or females. And there are three major genetic abnormalities and a bunch of extremely rare forms. But the three major genetic abnormalities that account for most of these 15% of cases are in the tau gene. It's called MAPT, but it's the gene that makes the tau protein. And those people are going to end up with a tau pathology causing their FTD. And then there's one called progranulin. Both of those genes are on chromosome-17, the tau gene and the progranulin gene. The progranulin gene is a special kind of genetic factor that basically leads to not having enough of this protein called progranulin. And for some reason, people can live 50 or 60 years like that being completely normal, and then they develop symptoms even though their whole life they've never had enough of this protein that plays a number of important roles in the brain and other body systems. And that is associated with the TDP-43 type of pathology in the brain. And then the third type is called C9orf72. It's an alphabet soup name, but it's on chromosome-9 and it is associated with FTD or ALS.

So we always take a family history when we talk to people about what happened to their parents, siblings, aunts, and uncles by asking not just about dementia, but about other conditions that might have led to debilitation, including weakness or ALS or something that might have been diagnosed as Parkinson's, because FTD can masquerade as some of

these other conditions, especially in prior generations. And so we really want to know, how old did your parents live? And were they debilitated by something brain-related in their later stages of life? If people's parents and parents' siblings lived into their 90s or even 80s and didn't have much of a problem with their brain, they probably are unlikely to have a genetic form running in their family because that would be very unusual. So these three genes are really not that common, but they're very much targets for trying to understand the underlying problems in FTD and what we can do to try to treat it. So they offer opportunities, just like the genetic forms of Alzheimer's disease, Parkinson's, and others do for identifying potential pathways toward treatment. There was just a new treatment approved recently for a specific rare genetic form of ALS that actually people are hoping might actually be applicable to other forms of the disease, too. So I think that's part of what we're hoping for when we're trying to recruit more people with these genetic forms of FTD to participate in studies, is that will be the key to the development of new treatments that might generalize across other forms of the disease.

BROOKS KENNY: Absolutely. Well, that's a perfect segue. I'd love for you to share with participants more about the Prevail study and really just the importance of clinical research and how we all can be part-- hopefully many of us can be part of some of these solutions.

DR. BRAD DICKERSON: Yeah, so there's is a consortium study called ALLFTD that I would encourage you to look up online if you want. That is a bunch of centers that are expert centers around the country that see people with any type of FTD once a year and do detailed assessments and then see them again every year. And the goal is to develop essentially the largest worldwide placebo group of people that are essentially living with the illness and being tracked very carefully over time with the idea that new treatments hopefully will improve what the course of the illness is compared to people that are just being followed for the so-called natural history of the condition. And so there are a number of clinical trials now that are targeting specific subtypes of FTD. Most of them are actually focused right now on the progranulin genetic type, which is quite rare. The estimates are there may be 60,000 to 100,000 people in the US living with any type of FTD. There may be 10,000 people at most, probably more

like 5,000 to 10,000 with the progranulin-related type of FTD, maybe even less common. But there are multiple trials, including the Prevail trial, that are trying to essentially replace this defective gene or the product that the gene makes so that they're boosting the levels of that protein that I said is lower than it should be. And in the long run, we hope we can give that to people before they have symptoms and delay or possibly even prevent symptoms.

So the Prevail strategy is to use a viral vector. It's called AAV, adenovirus vector, which is a way to safely deliver genes that are healthy genes to the body in people who have abnormal copies of those genes. And we have several FDA-approved medications that take advantage of this biotechnology, including treatments for hemophilia, muscular dystrophy. So this is a proven technology that works for these rare genetic diseases that are associated with a single gene mutation. So there are multiple different strategies, including Prevail strategy to try to do this for people with the progranulin genetic form of FTD, and partly because it's hard to figure out how to recruit those people because it's so rare. A number of other companies have sponsored free genetic counseling and testing for people with a diagnosis of FTD, and there are links to some of those on the AFTD's website. And so the goal is to try to help find people with this form of FTD so that they can try to be recruited for the trials. Right now, they're just looking for symptomatic patients, people with symptoms. In the long run, we're going to be looking for people that don't yet have symptoms. But right now, part of what they're trying to do is figure out if the treatments are safe. And if they are boosting the levels of progranulin in the way that we think they should in order to work. And there are other so-called biomarkers that are being tracked to see if they're improving along the way. And the initial preliminary study looked promising when it came to some of the correction of abnormalities of the biomarkers that we want to see in people that are getting successful treatment. So we don't yet know whether the people that are the first 13 people that got that treatment, if it's going to help them in the long run. But it's looking promising with regard to beginning to correct the biological problem.

BROOKS KENNY: Fantastic. I can't believe how quickly our time is going. And every answer is so chock full with such amazing content that I know

people are gaining so much knowledge today. Can you speak briefly about what are the treatment options right now for FTD, and maybe giving our community some insights into what can you do if you have a diagnosis? Are there lifestyle things that can be done to ensure the highest potential quality of life? And then I'm going to get to some of your questions in the chat.

DR. BRAD DICKERSON: Yes, yes. And I will just say that if you go on the AFTD's website, there's a list of centers of excellence that you can look for through by state. And if you have concerns about your own genetic risk, which a lot of people voiced, I think, the best thing to do is to reach out to the closest center of excellence to you and find out what you might be able to do in order to figure out what your genetic risk is. It may not be possible to do, because if you don't know what the biology of your family member with FTD was, then it's hard to know what to even test for. But the centers of excellence are really the fountains of knowledge that you should connect with. Because even if you can't get the answers for yourself right now, there are often studies that people can participate in of one sort or another to try to take advantage of cutting edge technology.

BROOKS KENNY: There are, I just wanted to highlight, for those of you in the chat, we're going to put all these resources in our email to you. But Dr. Dodge has been putting resources from AFTD, exactly what Dr. Dickerson was just explaining. So we'll make sure you have it in the follow-up, but definitely hope that you all use those resources. Sorry, back to you.

DR. BRAD DICKERSON: No worries. Thanks. Yeah, I think it's great to get the guidance that the AFTD can offer for a lot of the very specific individualized questions that people have. So in terms of treatment, I like to think about the idea that all of these conditions are treatable from the big picture perspective. Meaning, how do you do the best you can to support people in optimizing their quality of life despite the challenges that they're living with. They're not yet curable. They're not yet possible to stop in their tracks. They're not yet possible to reverse. They're not even possible yet to slow down. We just had the very first examples of that in any neurodegenerative diseases with the new approved treatments for Alzheimer's. And a lot of people talk about them as modest, which may be

true, but it's slowing down that condition. And this rare genetic form of ALS.

But all the other neurodegenerative diseases have no way of slowing them down, unfortunately. But there's a ton of research going on to try to change that. And I think we're really seeing the tides turn for the first time, which is encouraging. And like I said, I think all boats are going to float higher because these diseases have a lot of relationships to each other. So the way I think about treatment is, I want to find out what are the most important symptoms that people are experiencing that are compromising their quality of life? And let's make a personalized treatment plan to try to figure out what is possible to do about those particular symptoms. So if a person has aphasia, one of the best things we can do is to try to get them connected with an experienced speech language pathologist who can try to work with them and often their communication partner, spouse, or adult child, or someone else to try to help them develop strategies to compensate for the difficulties that they're having communicating. It's not like you can help a person recover from the problem like you can when they've had a static brain injury, like a stroke or head injury. It's more like you're helping them develop strategies to compensate for the difficulty. And their care partner also has to learn those strategies as well.

And then there are some types of symptoms that respond to medication therapies like some patients with FTD have compulsive types of behaviors where they do the same thing over and over again. Some have disinhibited types of behaviors where they've lost their filter and they do things that they shouldn't be or say things that they shouldn't be. And some of those types of symptoms can respond to certain classes of antidepressants or other medications that are often used to treat psychiatric symptoms. And there are trials of those, but there are also trials that have been completed that showed some degree of success. They often won't make those symptoms go away, but they may take the edge off of them.

And then there's the behavioral strategy approach, which one approach is called the DICE approach, which you can Google and get a website by several psychiatric practitioners that have developed this program that applies to patients with any kind of cognitive impairment or dementia that

are having different kinds of behavioral symptoms that you might want strategies to try to address. And then I think the other thing is support for the patient, family, and other people that are close to them. And that may come from a social worker, that may come from a community agency like AFTD support group or an Alzheimer's Association support group. may come from an Area Agency on Aging or an adult day program. But finding out what the local community resources are or the resources that may be accessible online, that can provide education and support is so critical because I think many people feel very isolated when they're living with one of these rare conditions. And sometimes if you have FTD and your caregiver goes to an Alzheimer's support group, the people have very different issues. So it's not one size fits all, although sometimes issues like losing driving abilities or other things that are more universal can benefit from a one size fits all approach. But it's better if you can try to get connected with a group that is for people as similar to your loved one as possible.

BROOKS KENNY: Yeah, that's fantastic. Really appreciate that and appreciate the underscoring both for the person living with disease and also their care partner and how to get that support. Just a couple questions from the chat before we start to wrap things up and show you all some resources. This was related to the treatment question. Someone with a primary progressive aphasia with Alzheimer's. The current Alzheimer's treatments are not indicated for that, even though they have an Alzheimer's etiology, correct?

DR. BRAD DICKERSON: Well, it's funny that-- it's a great question because no one with those characteristics was included in the trials, because the trials were meant to show that the treatment works. And in order to do that, you need to measure the most common symptoms that people have, which are memory loss, and so forth. So they specifically excluded people with so-called atypical forms of Alzheimer's. But because this treatment, these treatments that are newly approved, are targeting a fundamental biological problem in Alzheimer's, we believe that there's good reason to think they might work. And we are treating people with primary progressive aphasia due to Alzheimer's with those treatments. We don't yet know if they're going to work, but we don't think we should

close the door because the biology is largely similar. You might get a different answer from different providers, but I think it's worth at least trying to connect with someone that has a more open mind about this, recognizing that there may be other medical system or insurance related issues that might be barriers. But I think we hope that the atypical forms of Alzheimer's, like progressive aphasia or posterior cortical atrophy due to Alzheimer's, which affects visual processing, we hope that those will be responsive, too, but we just don't know yet.

BROOKS KENNY: Got it. A specific question about the PET scan you mentioned covered by Medicare. Is it a particular type of PET scan?

DR. BRAD DICKERSON: Yeah, so the most widely used PET scan is a glucose PET scan. It's basically a sugar. It is radioactive sugar because the brain's only source of fuel is glucose. And so what it tells you is what parts of the brain are not functioning properly, and that can be due to any cause. So that's called a glucose PET scan. And it's been approved, Medicare reimburses readily for it. Like I said, many private insurance companies, although this is getting better, too, give you a little harder of a time. But it's a very useful test to evaluate for any kind of condition that could be causing a person's brain to not function properly when they have cognitive impairment. So there's good evidence that it's helpful for diagnosing FTD, diagnosing Lewy body disease, diagnosing less common rarer conditions. So I would encourage-- and it tends to be ordered by specialists. I would encourage you to talk to a specialist about it. There are other types of PET scans that measure things like amyloid plaques in Alzheimer's or tau tangles. Those are becoming available now, but they're not as useful or not particularly useful at all for people with FTD. They may tell you that you don't have Alzheimer's, but they don't tell you that you have FTD.

BROOKS KENNY: Got it. I am torn because I want to ask you one more question. So I will quickly before we turn to resources. I'm going to combine some of the questions in here. A number of folks highlighted pretty strong family history of different neurological diseases, and kind of in this common thread from our conversation today, talking about empowerment and getting people to go to their doctor and ask for these

tests, how would you advise the community if you have a strong history, maybe you have a genetic marker, maybe you don't, like what is that conversation with your primary care provider and what's the best way to ensure you get into that diagnostic funnel?

DR. BRAD DICKERSON: Yeah, it's difficult because if you bring up family history with primary care doctors, they may put that in for things like breast cancer, colon cancer. They may really focus on that for certain conditions. But if you talk about dementia or Parkinson's, they won't know what to do almost universally. So I think more and more there are neurology and sometimes psychiatry programs at university hospitals that are offering brain health clinics. And the idea there is if you may be at elevated risk for a condition that ran in your family or at least more than one member of your family had, it might be possible to try to optimize resilience, even if we don't know exactly what your risk for it is. And so Mass General offers this. Beth Israel offers this. There are a growing number of academic medical centers that are offering so-called brain health clinics that are trying to help people when they're concerned about their own risk. I mean, the most part, if you read the Lancet Commission Recommendations on Modifiable Risk Factors for Dementia, which gets updated most every year, they talk about the major risk factors that you can actually do something about that would lower your risk for dementia regardless of what type it was. And those seem to apply across the board. So I would encourage people to look at that if they're interested in more detail.

BROOKS KENNY: I agree. I wait for that to come out and read it. And those are the things I forward to my friends and family. Well, thank you. While we pull up the slides, I just want to summarize some of the key themes that we heard today. I think first and foremost, I'm feeling this need as a community for us to continue having these conversations. There are things we can do. We can join clinical research studies. We can look at universities for more resources from providers. We can start asking questions when we see something in ourselves or in our loved ones.

This is the Prevail study that we had mentioned. The link is in the chat, and it'll be provided in the email. You can see that this gets to the

genetic conversation that we've been having around, how can we really understand the genetics of FTD and empower the research community to identify new treatment options? So definitely want folks to feel empowered that they can take action.

We can move to the next slide. And this is where certainly want to focus and invite Sharon from AFTD if you want to bolster any of my comments here. But obviously, AFTD is here to support this community. As I said, it's FTD Awareness Week and they are shedding light on this often misunderstood disorder. I hope today's session really brought more light to it for all of you. But they have a helpline. They have support groups. They have a lot of information about genetics. They have tons for researchers and then an annual conference for education. And they've just been such a wonderful partner to us at BrightFocus Foundation. And I think it deserves to be said that just like the research community needs to continue to collaborate, to learn from the lessons in the lab and in the clinics, we as nonprofit organizations need to continue to collaborate so that we can lift all of our collective voices. So I want to just, on behalf of BrightFocus Foundation, again, thank the AFTD for their partnership today.

We at BrightFocus Foundation also have a number of resources available to you in the area of Alzheimer's disease, macular degeneration, and glaucoma. You can visit us at Brightfocus.org/ZoomIn, and you can look at many, many episodes. I heard a lot of folks in the chat and in the pre-questions talking to us about Alzheimer's treatments and how is Alzheimer's diagnosed. And we actually have done a lot of work and posted a lot of expert conversations like this one on our website. So I welcome you to go there. And then these are our free publications which we're happy to send to you.

And lastly, just as a reminder, we will be doing these episodes regularly every month, sometimes twice a month. And so we want to hear from you. Our mission is to serve the community around these diseases. So please don't be shy. Email us, follow us on social media, engage with us, and let us know what other topics you'd like us to cover.

In October, we have two sessions planned. One is the Zoom In on Clinical Research, and we're going to be highlighting the START Study, which is

testing an oral capsule that may protect brain synapses. And so we're going to dig into that. And we really got this idea from all of you because you were raising your hands and saying, I want to understand what is a trial? How do I get involved in one? It's so interesting to us because in cancer, clinical trials are often the gold standard and people know about them and ask if there is one. But we have to continue to bolster that in Alzheimer's disease. And so we've decided to make this a regular part of our series. And you all are the reason why, because you asked for it. So we're happy to share. And then we're also going to be talking about how we can learn more about the diagnosis of dementia with a particular focus on Alzheimer's disease. And that's next month as well. And that is with Dr. David Holtzman, a renowned expert on the topic. And we know with promising treatments here now, diagnosis is really important. The earlier we can have it, the better. And so hopefully you all will register and tune in. And don't forget to share these registration links as you get them with your families. I think that one way we can break through stigma is to start these conversations sooner and having them more often. And sometimes if you come to an episode like this, it's a little easier maybe at your next holiday gathering to say, I was tuning in to this episode about diagnosing FTD and I learned some things that I didn't realize. Or it's just an easy thing, like my dad always calls me and says, I read this article in the newspaper. And that oftentimes will spark a conversation. So I encourage you to share this with the community around you.

And again, on behalf of BrightFocus Foundation and AFTD, we want to thank Sano Genetics for making today possible. And we want to sincerely thank our expert, Dr. Dickerson. I am just personally grateful that you're out there doing all the work that you're doing on behalf of all of our brains. So thank you for what you do, and thank you for being with us. I hope you can join us on a future episode.

DR. BRAD DICKERSON: Thank you, Brooks. Thank you, everyone.

BROOKS KENNY: OK, bye for now. Thank you so much.

Resources

BrightFocus Foundation: (800) 437-2423 or visit us at BrightFocus.org. Available resources include—

- Prevail Therapeutics FTD Program - https://tinyurl.com/2uheyvkm
- ALLFTD consortium study - https://www.allftd.org/
- DICE behavioral strategy approach - https://diceapproach.com/
- Lancet Commission Risk Factors for Dementia - https://www.thelancet.com/infographics-do/dementia-risk
- AFTD Resources:
  - AFTD HelpLine: 866-507-7222 or info@theaftd.org https://www.theaftd.org/aftd-helpline/
  - Support Groups: https://www.theaftd.org/find-support/
  - FTD & Genetics: https://www.theaftd.org/what-is-ftd/genetics-overview/
  - No-Cost Genetic Testing: https://www.theaftd.org/ftd-genetics/genetics-no-cost/
  - For Health Professionals: https://www.theaftd.org/for-health-professionals/
  - For Researchers: https://www.theaftd.org/for-researchers/
  - AFTD Annual Education Conference May 1-2nd in Denver, CO sign up here: https://www.theaftd.org/education-conference-2025/
- What is Frontotemporal Dementia? https://www.brightfocus.org/alzheimers/article/frontotemporal-dementias#

- What Are the Stages of Frontotemporal Dementia? https://www.brightfocus.org/alzheimers/article/what-are-stages-frontotemporal-dementia

- Symptoms of Frontotemporal Dementia https://www.brightfocus.org/alzheimers/article/symptoms-frontotemporal-dementia#