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

How Much Forgetfulness is Too Much?
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Transcript of Zoom with Ronald C. Petersen, MD, PhD
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Please note: This transcript has been edited for clarity and brevity.

NANCY KEACH: Welcome, everyone. Good morning. Good afternoon. Good evening. I'm going to welcome you today to Zoom In on Dementia & Alzheimer's, "How Much Forgetfulness is Too Much?" We have a great guest today

I'm Nancy Keach. I work at BrightFocus Foundation, who is the host of these Zooms. BrightFocus Foundation funds scientific research worldwide to understand, treat, and cure macular degeneration, Alzheimer's disease, and glaucoma. And we have funded over $300 million of research over 51 years for these diseases. And so we're delighted today to have you on for this episode. I believe it is the 20-somethingth episode of Zoom In. And I want to thank the educational support from Lilly, Biogen, and Genentech in making this program possible.

As I mentioned, we received about 90 questions, and they are on various topics. And so if your question isn't answered today because it isn't on today's topic, please note that all of these episodes are on our website, on YouTube. They're free. They're an hour each with the world's greatest experts on Alzheimer's and dementia. And so if you ask something about new diagnoses, or a new diagnosis technology, or the stages of Alzheimer's, or something in particular that you don't get covered fully, I promise you, we've covered it fully in one of these episodes, so please use them. Please refer to them.

I am delighted to see you all. And now I am delighted to introduce Dr. Ronald C. Petersen. He is a neurologist at Mayo Clinic, where he focuses on investigations of cognition in normal aging, mild cognitive impairment, and dementia. Dr. Petersen and his colleagues evaluate cognitive changes in normal aging, as well as in a variety of disorders involving impairment in cognition, such as Alzheimer's disease, frontotemporal lobar degeneration, and Lewy body dementia. Dr. Petersen directs the Mayo Clinic Alzheimer's Disease Research Center and the Mayo Clinic Study of Aging, both of which involve the study and characterization of aging individuals over time with an emphasis on neuroimaging and biomarkers. And I am absolutely delighted to welcome my friend and colleague, Dr. Ron Petersen. Thanks for being here.

DR. RONALD C. PETERSEN: Well, thanks, Nancy. Thanks very much for inviting me. I look forward to our discussion today.

NANCY KEACH: And I have to mention that Dr. Peterson was one of the first people I met years and years ago when we were working on a film about Glen Campbell. I don't know if some of you have seen that, Glen Campbell, I'll Be Me. And Dr. Petersen was the doctor who helped to scan and diagnose Glen Campbell, and that is in that movie.

So we've done about, I said, 20-some odd of these episodes and have had about 1,750,000 views of the programs. And so we thought today would be actually a good time to go back to the basics, to some of the questions that are most often asked and people are most wondering about. Hence the title, which is a little bit unanswerable, but Dr. Petersen is going to try to answer it today. So I'm going to kick us off with two questions that

were submitted, Shirley from Hermitage, Pennsylvania, "What is the first thing I need to do if I'm becoming forgetful, testing, blood test, MRI, what?" And another one from Larry in New Hampshire, "Is there a reliable test to check on whether forgetfulness is simply normal aging versus Alzheimer's? Thank you."

DR. RONALD C. PETERSEN: Well, Nancy, these are excellent questions to start off the discussion. And I must apologize when I put up a title like "How Much Forgetfulness is Too Much?" I don't answer the question at the end of the day because it is a vexing problem. And it's very common these days. So as a clinician, it's not at all uncommon for people to come into the office aging 60s, 70s, 80s, and say, gee, doc, I'm not remembering as well as I used to. Is this Alzheimer's disease? And I must say, it's not a trivial question.

So we do recognize that there is some forgetfulness and inefficiency in thinking that goes with aging. So I think all of us have trouble with names of people. I used to work with that guy, ran into him in the grocery store, and say, hey, chief, buddy, how you doing stuff like that because I can't remember it's Bill, until I get three aisles away and say, that's Bill, how could I forget him? So hopefully, those kinds of incidental forgetfulness episodes are part of aging, I hope. And similarly, you go into a room, now, what did I come in here for? That type of stuff. But when we start to experience forgetfulness for events, things that we usually would have remembered, important things to us. So I have a luncheon engagement with my buddies on Tuesday at 1 o'clock, I don't show up. Or I've got a tee time on Thursday at 9:00 AM, I don't show up. Again, that kind of happens periodically. You get distracted.

But when that becomes a pattern, so now I'm forgetting things that I formerly remembered fairly easily last week, it happened this morning, it's going to happen again next week, it might deserve our attention. First thing might be to talk to your family, friends, people around you, have you noticed anything? Am I more forgetful than I used to be? Again, doesn't mean it's abnormal but let me know. And then have that discussion with your primary care physician. Go in and talk to them and say, gee, I think I'm a little more forgetful. My family's noticed that

I'm starting to forget important information. Is this something to be concerned about?

The primary physician then may look at your general medical picture, what's going on in your life, stress, anxiety, what medicines you're on for your blood pressure, for your bladder problem that may actually impact your memory and see if there are other factors that could be contributing to it. You and your doctor can decide then, should I pursue this further, should I be referred on to a neurologist, or neuropsychologist, a psychiatrist, geriatrician, somebody of that to take it to the next step? So I think that it's important to recognize this. Don't panic about it. But try to see if there is, in fact, a pattern of forgetfulness that is new for you, different from what you've been experiencing in previous months and years.

NANCY KEACH: You touched on something that I was going to bring up much later, but there are other medications and issues that can mimic signs of mild cognitive impairment. Is there anything in particular people should think about right away?

DR. RONALD C. PETERSEN: There are some medications, sometimes over-the-counter medications, things that we might take because we have a cold. So we take something like Benadryl, diphenhydramine, that, in fact, dries us up and may help us with our allergies, but it does have what are called anticholinergic properties. So it blocks one of the chemical systems in the brain that's involved with memory. Another common one I mentioned are bladder medications. Many older folks have trouble with a little bit of incontinence, a little bit of urgency, things of that nature. Our urologists would say, well, we can help you with that. Here's a medicine, Detrol or something of that nature, it has anticholinergic properties, that's how it works on the bladder. But sometimes, some of that will, I shouldn't say leak into the brain, but will get into the brain in small amounts. But these medications can be very deleterious to your memory function. So it's a good idea to survey medicines you're using, not only prescribed medicines, but over-the-counter medications. And the combinations of them may actually have some adverse effects on your memory and thinking.

NANCY KEACH: And so my mom's 95 now and she's been diagnosed with mild cognitive impairment. What I see with her and a lot of people is that one of the first signs is asking the same question. And a lot of times we're talking about memory, but you just asked me that five minutes ago kind of thing is often a recognition from people that something is wrong. And the other thing that I hear quite commonly is like suddenly making mistakes with your checking your bank account or not paying bills, those types of things. So is that different from the normal forgetfulness of aging?

DR. RONALD C. PETERSEN: Well, Nancy, I think those are signs of what I was thinking that might be a little more impactful. So again, we may get distracted. What time are we going to dinner tonight? And you ask your wife, and she says, oh, 7 o'clock, we're going to meet the Wilsons. OK, great, half an hour later, now, what time are we going to dinner? Again, a little bit of that. But when that becomes a repetitive behavior, you just asked me that, yesterday, the day before, that's a question that I often ask of the family members or somebody who accompanies the patient into the office, is he or she repeating himself, and is that happening more frequently now than it did 6 months ago, 12 months ago, 2 years ago? Because it's a metric that that recent memory function may be failing a bit.

And I say, is the duration between these questions shrinking? So you just asked me an hour ago, half an hour ago, 15 minutes ago. So I think those can be indices. Again, it doesn't mean Alzheimer's disease. But it does mean that our recent memory functions may not be as good as they used to be and may deserve some attention. And similarly, checkbook kinds of things, that may be more in the realm of attention, concentration. But if you pay bills twice or you forget to pay bills, again, that's an index of recent memory. Doesn't mean you've got Alzheimer's. But it's worth noting to your family, noting to your personal physician.

NANCY KEACH: I have a good question from YouTube from Anker, "I'm having trouble with recall, but most times, I will remember a few minutes later. It is usually nouns and names. It is something that has been happening more often than in the last couple of years." So what would you say?

DR. RONALD C. PETERSEN: It's sort of, again, not diagnostic but

suspicious. You're observing something that's important. It's happening more frequently now. It's kind of recent memory and so a type of forgetting that can be indicative of a problem. Usually, this implicates the part of the brain that's involved with laying down new memories and recalling recently experienced events, the hippocampus, the medial temporal lobe part of the brain. Now, it shrinks in aging so some of these things happen with aging, but it shrinks more dramatically in Alzheimer's disease and other disorders. So it is the part of the brain that's involved in exactly these functions, kind of keeping track of what happened yesterday, the day before, and recalling these recent events. So I think what you're asking about is one of those signs that maybe, you should pursue it a little bit further. Again, it doesn't mean it's nasty but it's worth further attention.

NANCY KEACH: I'm going to backtrack for a second, and I'm going to ask you the most commonly asked question that we ever get, and I'm going to add something to it. The most common question we ever receive is, what's the difference between Alzheimer's and dementia? To add to that, what's the difference between mild cognitive impairment, Alzheimer's, and dementia?

DR. RONALD C. PETERSEN: Sure. Very, very important line of questions because I, too, get those kinds of questions all the time, do I have Alzheimer's disease, or do I have dementia? And so we have to back up and say, what do we mean by these terms? Well, how do we define Alzheimer's disease these days.

And generally speaking, when we approach it, we talk about the clinical picture, the so-called syndrome, the clinical syndrome of what's going on, how are you remembering, how are you thinking, what's the clinical picture. And that's on a continuum from, say, cognitively unimpaired to maybe subjective cognitive decline, meaning I'm still normal but I think things are changing to mild cognitive impairment is the next stage of clinical impairment. And then dementia is the final stage, mild, moderate, severe dementia. So what do we mean by those?

Well, we've talked a little bit about cognitive aging, subjective cognitive decline, I'm aware that things are changing. Mild cognitive impairment is an abnormal clinical state that usually means, I'm not remembering as

well as I used to but maybe not as well as I ought to. That is, I'm having this forgetfulness that I described earlier of events that I formerly would have remembered, but now I am forgetting them on a regular basis. Family and friends around me have noticed I'm not remembering as well as I used to. But everything else is OK. I'm driving. I'm paying my bills. I'm doing my taxes. To the casual observer, I look normal. But I know, my family knows things are changing a little bit. But it's not that you're losing your dependence. You really can still function independently, maybe less efficiently. It'll take you longer, but you can do everything.

However, when you cross that boundary to now my cognitive problems are impairing my daily function so I can no longer do what I formerly did, paying the bills, even operating the computer and things of that nature, I can no longer do them by myself, I do need assistance, that's when we get into the dementia range and mild, moderate, severe is that.

So that's the clinical continuum, again, the syndrome. So we make that diagnosis first, where are you on that clinical spectrum. Once we've made that call, then we say, OK, now, what's causing that? If you have mild cognitive impairment, what's causing it? It could be Alzheimer's disease, but it may not be Alzheimer's disease. We mentioned earlier drugs that are treating other medical problems may have side effects that affect your memory. A common one is a sleep disorder. So we do take an extensive history now on people's sleep hygiene, how well they're sleeping, do they awaken during the night, do they snore, do they have apneic spells where they gasp for air in the middle of the night? Because it has been the case that if we identify obstructive sleep apnea that had not been characterized previously and you treat that, the mild cognitive impairment may go away. You may go back to normal because your syndrome of mild cognitive impairment was due to a medical problem. We treat that, the person goes back to normal.

So we ask the questions, what's causing the mild cognitive impairment? We go through all those medical issues, all those medicine issues, and things of that nature. But if we don't find anything that's obviously causing it, then we may go down the pathway of could this be Alzheimer's disease, and we start getting some of the biomarkers, and we can talk about that a

little bit later.

But it's important to keep the clinical picture, the clinical continuum, the syndromes and then the underlying causes of the syndromes separate. So is dementia Alzheimer's disease? It may be. But it may be the dementia stage of the underlying Alzheimer's biology or the mild cognitive impairment stage of the underlying Alzheimer's biology. So they're not synonymous, but they often do go together and that causes confusion for a lot of us.

NANCY KEACH: And I'm going to, in a minute, get to some of the other types or other causes of dementia. But a question I get a lot is so let's say you're diagnosed with the mild cognitive impairment and the other things are ruled out and this is actual mild cognitive impairment. Does that always progress into Alzheimer's or some type of dementia?

DR. RONALD C. PETERSEN: Not always, no. And again, as we said, if you find a treatable cause, you can actually reverse it. And sometimes, depending on the cause, it may progress very, very slowly, like we can talk a little bit later about another neurodegenerative condition called TDP-43 or so-called LATE syndrome, that is a different protein in the brain but affects memory, looks like Alzheimer's disease, but it's not.

However, if, in fact, we diagnose the syndrome of mild cognitive impairment, and then all those rule out stuffs are negative, and we say, OK, let's do some of the biomarkers now that will specifically identify Alzheimer's disease as a cause, and they're positive, then we have mild cognitive impairment likely due to underlying Alzheimer's disease. Then we think that it will progress on to dementia at a rate, varies a good deal, 10% to 15% per year is a ballpark figure. And studies have documented that that's kind of the rate of progression. Again, they can go much faster than that, go much slower than that. But in general, if mild cognitive impairment is due to underlying Alzheimer's disease biology, then it probably will progress at that rate.

NANCY KEACH: We've gone around that there are other causes of dementia besides Alzheimer's. I'm going to start with Barbara from Augusta, Georgia, "Define and describe symptoms of vascular dementia." And then a similar from Gail in St. George, Maine, "My husband is

diagnosed with Alzheimer's/vascular disease. Is it true that the vascular disease proceeds much faster than Alzheimer's? His decline seems rapid and odd since his diagnosis three years ago." So let's start with vascular. And I don't know how common is that, what are the differences, and go into some other types of causes of dementia.

DR. RONALD C. PETERSEN: Actually, Nancy, it gets at the broader issue of that. We've already addressed a bit, that is you have the clinical syndrome that could be due to a variety of causes. One of the main causes is Alzheimer's disease. What is that? The amyloid plaque protein, the tau tangle protein. But there are other factors that occur with aging that are very common that can happen with Alzheimer's disease, and vascular disease is one of them. And here, of course, there's a range of vascular disease. We could be talking about a stroke, where if somebody has an infarct, a loss of blood supply to a certain part of the brain, that part of the brain doesn't work very well. So if it happens to be one of the memory circuit parts of the brain, the person might get forgetful. Usually that happens rather abruptly when somebody has a stroke.

But there's also another form of vascular disease, subcortical vascular disease, vascular cognitive impairment that is due to small vessel disease, tiny blood vessels. They don't cause a major stroke, so I'm not losing control of my arm or losing vision. But it starts nibbling away at brain structures and brain connectivity patterns. And it can produce cognitive impairment over time in a gradual fashion as the vascular disease builds up in the brain.

And again, Alzheimer's disease and vascular disease can coexist. So your second caller was saying that-- asked about Alzheimer's disease and vascular disease. You've got two factors going on now. So in general, the more neuropathology you have active, the faster the disease will go. So it could be a combination of the two. But they're very variable. Both the Alzheimer's disease can be variable. And the vascular disease component can be variable as well. But in general, if you have both of them, they probably will progress more rapidly than either alone. And you treat those somewhat differently. A vascular disease, treat the risk factors, hypertension, smoking, diabetes, et cetera. The Alzheimer's disease, we

have other treatments for that. So it does matter that you do try to tease it. It can be difficult to tease out also how much of your clinical picture is due to one factor or due to the other factor. And that comes down to a judgment call on the part of the clinician who is evaluating the situation.

NANCY KEACH: In your introduction, it said you also study Frontotemporal Lobar Degeneration or I think FTD is how a lot of people hear about it. It's the disease Bruce Willis seems to be suffering from and that's in the news a lot. And then there's Lewy body dementia, which is likely what Robin Williams passed from. Can you talk about these different causes of dementia and then the underlying-- let's talk about also what is a biomarker, how are you distinguishing one from the other and then deciding that these can be treated differently?

DR. RONALD C. PETERSEN: Sure. So going back to our original discussion of the clinical picture, so we look at the clinical picture, normal, subjective, cognitive decline—

NANCY KEACH: Sorry, Ron. When you say the clinical picture, can you explain what that means, the clinical picture?

DR. RONALD C. PETERSEN: The set of symptoms that the person presents with. So is it memory? Is it behavior? Is it visuospatial, language? The clinical pattern that the clinician will assess in the patient. Most patients come in with, gee, my memory is not what it used to be. Often, they're right. But they could be saying memory and they really mean language, I'm having word finding, I'm not understanding what people are saying. I'm having trouble translating my thoughts into words. That's a language problem. They may call it memory, but, in fact, it's a language problem.

So we do that clinical spectrum analysis along the way. But also, there are qualitative features of that. So it may be memory in one person, but in another person, it may be behavior. The person is starting to do things that are out of character for this person. It's like a "personality change." Now they're saying inappropriate things, doing inappropriate things in public, maybe using language that they never would have used before, commenting on the physical appearance of another person in public, never would have done that before, those are what we call behavioral

features. And while that can happen in Alzheimer's disease, it's not common, especially as the presenting feature.

So if we see those kinds of behaviors, that clinical picture developing with behavior more than memory, we think, gee, something like frontotemporal lobar degeneration may be in play here because, as the name describes, the frontal lobes of the brain, the temporal lobes of the brain are more involved than other parts of the brain.

What does the frontal lobe do? Well, the frontal lobe manages our behavior, our personality. The appropriateness or inappropriateness of your behavior can be regulated to a degree by the frontal lobes of the brain. So if now the pathology, different proteins than Alzheimer's disease, but let's say, a tau protein or a protein called TDP-43 builds up in the front part of the brain, then behavior becomes the presenting symptom of that person. And that takes us down a different pathway in terms of evaluating. And you mentioned, Nancy, what are biomarkers. I'll get to that in a second. So it could be that the clinical picture of is it behavior, is it memory, is it visuospatial skills, is it language will tip the clinician in one direction or another.

You mentioned Lewy body dementia. Lewy bodies are seen in Parkinson's disease most commonly. So sometimes people with cognitive issues, memory problems, will come in and the clinician will see that, gee, this is more a problem of speed of processing, visuospatial skills, the person's getting lost in familiar environments, getting lost in his or her own home. It's kind of unusual, but that's a visuospatial. When you see that in the setting of what might look like Parkinsonism on the examination, so the person is stiff, their face is not animated anymore, they may or may not have a tremor but they lose their balance when they're walking, these are subtle signs of Parkinsonism. And you put those together with a certain pattern of cognitive impairment and it makes the clinician think this might be a Lewy body disorder rather than Alzheimer's disease.

And so then we start looking at what are the biomarkers, the biologic tests that give us an indication of what's pathology in the brain, what's going on in the brain. So Alzheimer's disease biomarkers, basically the two proteins

that are abnormal in Alzheimer's disease are amyloid causing the plaques and tau causing the tangles. Well, we can look at those proteins pretty accurately now. We can do imaging tests, PET scans that will actually identify the amyloid protein in the brain, the tau protein in the brain. We can look at spinal fluid. We can do a lumbar puncture and look at these abnormal proteins in the brain, amyloid and tau, reflected in the spinal fluid. We're getting to, and maybe we can talk about this a little bit later, maybe blood tests. The field is advancing now and some of your other speakers in this series have talked about blood tests that may actually reflect the amyloid and tau proteins. So those are exciting biomarkers that are evolving in Alzheimer's disease. I think we're more advanced in Alzheimer's disease than we are in some of the other disorders.

So I mentioned Lewy bodies and Lewy body dementia, Parkinson's disease, well, we can see that to a certain extent with, for example, on a spinal tap now, a lumbar puncture, you can get an index of the protein, alpha-synuclein, that causes Lewy bodies. You can do skin biopsies that actually detect whether or not the Lewy bodies may be present in the brain. And we can do another kind of a scan, a nuclear medicine scan called a SPECT scan, a CAT scan, dopamine transporter scan, because that particular chemical in the brain is abnormal. So we can do biomarkers that give us a clue is there a Lewy body component going on. Some of the other ones are a little more obscure. We talked about vascular disease already. But there's this thing I mentioned, TDP-43, we don't have a good test for that right now, a good blood test, spinal fluid test. Sometimes, there are patterns on a glucose PET scan, which reflect the metabolism in the brain, that can give us a clue. But we don't know that for sure.

So we try to put all these different biomarkers together with the clinical picture and we come up with a diagnosis of this is likely Alzheimer's disease, frontotemporal lobar degeneration, dementia with Lewy bodies based on the clinical picture, which is different in each of these and the biomarker profile. It's becoming more and more complex. But I think it's becoming more specific too. We used to just call these dementia in the past. Everybody's got Alzheimer's disease. But now we realize that only some people have Alzheimer's disease. There may be these other dementias that are equally prevalent.

NANCY KEACH: So when we first talked about doing this, we had a title

of "why is it so hard to get a diagnosis" or something like that, and I think you're getting at that, in that there are underlying biological differences. You might have a Lewy body protein or different types of proteins or little strokes, mini strokes. So you have something different going on the biological level with these different types. Then you also have behavioral symptoms, some of which may be the same and some of which may be different. So you're trying to determine, and I'm going to come back to that in a second. But I just want to go back to something I wanted to say at the beginning, because you've mentioned it several times, that in detecting, you're looking for a change, something that didn't used to happen that's happening a lot. And this is why in diagnosing, a partner, or a family member, a partner, a good friend is so important, I think, to the diagnosis because they can make observations, is this happening in differently than before. And so it's not just like, oh, come along with me because I want you to be there while I'm at the doctor's office. That person is actually helping to establish—

DR. RONALD C. PETERSEN: Extremely important. The person who comes in with the patient is very important to give exactly what you're saying, Nancy, observation, is this the same or different from this person six months ago, a year ago, what's the nature of these changes. Because one of the things that happens in these degenerative diseases of the brain is we lose our own ability to look at ourselves. It has a name called anosognosia. And it's not necessarily a psychological defense mechanism. I don't want to go there because I'm afraid I've got it. That may be part of it. But often, it's the part of the brain that's involved with the disease process precludes us from our ability to look at ourselves.

So I mentioned earlier with the behavioral form of frontotemporal lobar degeneration, the frontal lobes are involved and the right side of the brain are involved in our ability to perceive ourselves. And sometimes, you'll get people who come in who are clearly impaired and you sit down and ask them, how are you doing? I'm fine. I'm A-OK. I've never been better. How's your memory? It's perfect and all that. And the family member is sitting in the background going, no, no, no, no, no, no, no, that's not the case. And again, the person's not trying to deceive the doctor. He or she just does not appreciate it. Part of the brain does not allow them to look at

themselves. And that can be difficult in a management situation because the person doesn't see there's anything going on. It's not like I have a headache or a pain in my belly. No, I'm A-OK. The only reason I'm here is because he or she brought me. They made me come. I'm fine. So that can compound the problem.

NANCY KEACH: I've always been fascinated with anosognosia, which I've heard the term lack of insight. And I remember, for example, with Glen Campbell, that the filmmaker who was making the film used to say to him, hey, Glen, how's the Alzheimer's? And everyone around him would go, [GASPS] you don't say that to him. And he'd go, I don't got no Alzheimer's, I've got old timer's. Because he knew he had Alzheimer's but he had lost the insight, as you're saying, into what that actually means for him or his family, which in some ways maybe is a blessing.

And I have a question, because I find this very fascinating-- Flo from Alexandria, Virginia-, "Do most patients recognize what is happening to them? My husband seems to be at peace and he has been on this journey for five years." And I think she's lucky. But maybe you can talk to that. Do most people know this is happening to them?

DR. RONALD C. PETERSEN: That's a difficult question do most because what's your denominator? What are you talking about? I think, in general, most people do appreciate that things are not going as well as they formerly did. I'm not thinking as well as I did. I'm not remembering as well. They may not appreciate the degree to which they're impaired. But I think most people do appreciate that something is going on. And of course, that can lead to anxiety, depression, and all other kinds of things that are treatable. We shouldn't ignore that because they can be treatable components of this process. I think most people do. But again, as we say, if the parts of the brain that allow us to look at ourselves are involved, they may not appreciate. So I think, in general, the answer is yes, most people appreciate it but often not to the degree to which they are involved.

NANCY KEACH: Before we leave this subject, I think I'm going to read three questions. Charlotte from Somerset, New Jersey, "I'm constantly writing notes as reminders and then too many, which is frustrating and makes me anxious. Is this a sign of dementia?" And from Wendell, North

Carolina, "It sometimes seems that my husband is not remembering, paying attention to what's just been said or following the context of the conversation... distracted?" And there was another one I wanted to read. Well, in any case, the one I was looking for is, yeah, Susan from Woolwich, Maine, "As a care partner, what is the best way to address repeated forgetfulness?" And where I'm going with this is so you have these symptoms that can be annoying, right? And you get angry. And so when someone asks you the same question over and over-- you said that there's treatments for anxiety and for the caregiver. There's medication for the patient. Let me hand that over to you.

DR. RONALD C. PETERSEN: No, no, it's a very relevant issue. And it's not at all uncommon that people feel guilty. My husband keeps asking me the same question. I just told you this. We're doing this, we're doing that. Then they feel guilty about getting frustrated that their husband is asking the same question. He can't help it because he forgets that he just asked it. So it is a stressful situation for caregivers. I think you just have to take a deep breath and try to answer the question politely, quietly, et cetera. And I think that caregivers need a break every now and then as well. I mean if this is a 24/7 job, it can be very stressful, not good for you, not good for your loved one either.

So I think these kinds of situations are quite common. And I think we do need to be mindful of the caregiver's health and mental health. And it may be that, yes, we can treat the patient with anxiety medications, depression medications. We have to look at the caregiver as well. Is the caregiver going down the road of anxiety, depression, guilt, whatever you want to call it? So I think caregiver health is very, very important for the quality of life of the patient as well. So I think it really is a dyad that needs to be handled together.

So, Nancy, one of the other earlier questions was, again, I'm keeping more notes. May not be the end of the world. A lot of us do. That's why Post-it notes were made, for us to use them. But again, if that pattern is excessive and is different from what it was a year ago or so, that might be an index that maybe we should take a little closer look at this.

And the other caller was saying, my husband seemed to not be paying

attention to me. So that can happen with aging. I think with aging, we cannot multitask as well as we formerly did, cannot keep as many balls in the air, if you will. So attention, I often tell patients that as you're aging, when you meet somebody new or some new situation occurs that you want to remember, stop, take an extra minute, pay attention to that. Now, your name was Bill Wilson, now, Bill Wilson, that type of thing, rather than when we're younger, we could pick these things up incidentally, and it goes along pretty well. But I think as we age, we have to pay a little more attention on the input side to make sure that we understand exactly what we're hearing, what we're trying to remember. And of course, if we can attach it to something we already know, a meaningful association, that can help us remember such that when we see that person again, we'll be able to come up with that individual's name. But inattention certainly can be part of it. And of course, it always comes down to husband and wife, you're not paying attention, you don't listen to me, and selective inattention. I don't want to go there if I don't have to. So my wife would have words about that. So let's just stop that.

NANCY KEACH: And I haven't brought this up in the professional context, but I hear often, and I have a lot of friends, when someone has moderate to more advanced Alzheimer's, they will often start to ask for a deceased spouse, when is Joe coming home? My dear girlfriend's mom started to ask about her cat. Where is the cat? The cat had died 20 years ago. And people really struggle with, do I say "Joe died, honey, Joe died and the cat died" or do I say, "oh, the cat's outside and it's coming back soon"? And I think there's a lot of guilt attached to that. People feel like, oh, I shouldn't lie to them. So I know it's different in different situations. What would you say there?

DR. RONALD C. PETERSEN: Yeah, it's not uncommon, again. And sometimes, we call these therapeutic fibs where we're saying, oh, I think the cat's just out in the yard. She'll be back in a few moments, rather than getting into, especially if it becomes emotional. You don't want to get into an argument. I sometimes think of it as the patient with the neurodegenerative disease is playing with a little different deck of cards than you are. So they may not be able to compute, may not be able to understand, follow the reasoning. So when you get into an argument

and say, no, it can't be because of this, this, this, person may not be able to process that. And as the emotions escalate, then the whole situation deteriorates.

So at the same time, you don't want to live in a masquerade world and all that, but these therapeutic fibs sometimes can be fine. And the reason that these happen is when, say, Alzheimer's disease as a neurodegenerative disease of the brain begins, it begins in that part of the brain, I mentioned earlier, hippocampus, medial temporal lobe, and that destroys recent memories, things that happened yesterday, a week ago, et cetera. But as the disease progresses around the brain, then older memories start to become affected as well. But often, they're preserved far into the disease, that is, where I went to high school, what happens when I was in college, and all that kind of stuff is remembered more easily than what I did last week. Again, that is the temporal grade of the disease process.

But as the disease progresses, even those older memories become less reliable. And there can be this element of what we call confabulation where the person tries to put a couple of the things together that really don't match. They don't make sense. But again, not arguing with the person. Or that some of these old memories come back like, gee, where's mom? Well, mom's been gone for 20 years. But you have to assess that situation and say, no, mom's been gone and maybe that's satisfying to the person. But if the person says no, no, she's here somewhere, then the therapeutic fib comes in, yeah, she just went next door but she'll be back in a little while. Change the subject, distract the person to get onto another thought process, and that can alleviate some of those symptoms of anxiety that can come up. But that certainly does happen.

NANCY KEACH: Yeah, I'd like to alleviate the guilt from people for telling therapeutic fibs because it's not a lie, as we say in a lot of cases. And I think Jane Kramer wrote in the chat, it's the same with telling someone they have Alzheimer's over and over again. That's a constant trauma. So I think, natural to get angry and frustrated but not always correct to try to be rational. And that's what I see, is when people resort to trying to be as rational as possible and that can really cause more stress, more anxiety.

DR. RONALD C. PETERSEN: Emotional escalation and the whole situation

deteriorates. That's right.

NANCY KEACH: Someone asked, and I think this also goes back to the symptoms, the anosognosia we were talking about. Someone asked, Barbara from Springfield, Virginia, "What's the connection between aphasia and Alzheimer's?"

DR. RONALD C. PETERSEN: So aphasia means that there's a language problem. So I'm having trouble interpreting, understanding either the spoken or the written word and/or I'm having trouble expressing myself verbally so I have more problems translating my thoughts into words. So aphasia refers to language processing in the broader sense. And there are regions of the brain that are more involved with language. Most of us, it's the left side of the brain that is involved with language, especially in right handers, but even left handers, it's the left side of the brain. So if for whatever reason the neurodegenerative process affects that part of the brain early or preferentially to other parts of the brain, then language problems will be the presenting feature of the disorder of the degenerative disease.

We talked earlier about FTLD, Frontotemporal Lobar Degeneration. I talked about the behavioral presentation. But there's also a language presentation or several language presentations where it's the language function that gets affected out of proportion to the other cognitive functions. And that can be very distressing because now the person may not be able to understand what you're saying to him or her. And again, that's a source of frustration. Or they're unable to express their own thoughts. They cannot verbalize what they're thinking. That's very frustrating to them. So there are language, speech pathology techniques that can be helpful. And if language is the only function involved, sometimes there are techniques that a speech pathologist can teach a person to get around some of those blockages in the language system. So don't give up on it. But it certainly can be a different form of a degenerative disease of the brain.

NANCY KEACH: I've seen music therapy be effective sometimes. And if anybody has seen the Gabby Giffords documentary after she was shot, but she couldn't speak, the music helped her be able to speak again.

DR. RONALD C. PETERSEN: Right. And, Nancy, you remember very well, like Glen Campbell, too, Glen had particular difficulty with verbal memory. So in the documentary that you, and James, and Trevor put together on Glen, he needed a teleprompter to sing the lyrics of songs he'd been doing for four decades. But there are other parts of the film where the teleprompter would just say, Glen play long guitar solo here, and he would go off by himself with his tremendous musical skill and play the guitar "appropriately" for the song for five minutes without any prompts. So different parts of the brain deteriorate at different rates. And in that instance, it was his episodic memory, verbal memory that was out of proportion to, say, his motor musical skills.

NANCY KEACH: It was so fascinating. Kimberly sorry if I'm destroying your name, and this is going to bring us back to where we were with the Lewy body, is it common to see someone suffering from Alzheimer's to be paranoid?

DR. RONALD C. PETERSEN: It certainly can happen. It happens usually later in the disease. But as you were saying, Nancy, it may be more indicative of another degenerative process, one involving Lewy bodies. So in Lewy body dementia, one of the earlier features may be behavioral, delusional, hallucinations, visual hallucinations. And these are interesting hallucinations. They're not "crazy" stuff. But in fact, I'm seeing a little boy over in the corner. He's sitting there. I know he's not real. I know there's no little boy here in the room. But it sure looks like him. And make sure you set a place for dinner in case he decides to stay. So it's sort of this reality that I'm seeing something, I know it's not real, but yet in my mind, there's something that's real about it.

So these kinds of things, delusions, paranoia that people are out to injure me, or harm me, or steal things from me, if that's an early feature, we think Lewy bodies. But it can be a later feature in Alzheimer's disease as well. So we all know about the stories of people who are in clinical care facilities, skilled nursing facilities, who may go room to room and steal things, one. Or I can't find my whatever, somebody has stolen this from me. So paranoia can be a part of Alzheimer's disease as well.

NANCY KEACH: I'm just going to mention, we have about nine minutes

left. So if anyone has a burning question, put it in the chat. We're going to keep going. But I just want to give you that heads up. This is something also we hear a lot, Ron, and something interesting for me, people ask the difference between brain fog from COVID and dementia. And also, I'm here in LA and experienced the fires. As you know, I lost our home. And I've noticed that since those fires and that experience for us, I'm experiencing a lot of brain fog just from having gone through that and being displaced. But long COVID is a thing and brain fog is a thing. Can you talk about that, the difference?

DR. RONALD C. PETERSEN: Yes, very real but very difficult to pin down as well. So again, I'll retreat back to our earlier discussion about what's the clinical picture of the syndrome. And I think most people by brain fog mean that I'm having a little trouble with my memory and maybe my attention is off. I'm not concentrating as well as I used to. So that might be the clinical picture of what's going on.

But now we're saying what's causing it. Could COVID have caused that or still be causing it? And that's an actively studied area, what's long COVID and the like. And it may very well be that the COVID process, when it affected the brain in an individual, did cause some inflammatory reaction in the brain that may continue on, may smolder for a period of time. So it may be that the inflammatory reaction caused by the virus is actually perpetuating and is affecting some of these parts of the brain that are involved with attention, concentration, and memory. That's a possibility. And certainly, in your situation in Southern California, I mean, you can imagine all the stress, the anxiety, as well as, and here I'm getting out of my wheelhouse, "the pollutants" that may be around that could be contributing to general physiologic function and brain function is a possibility.

So I think these are very real, but they're very difficult to tease out as well because there aren't often biomarkers for this. So I can't measure your blood. I can't do a brain scan that tells me, oh, you've got brain fog due to COVID. We can't do that. So it really comes down to a clinical characterization of the person and a clinical judgment as to whether, in fact, these are neurologic symptoms that are due to some of these other

conditions.

NANCY KEACH: Well, that's interesting. I see Amanda just put in the chat that there's an article today about long COVID dementia and environmental pollutants. She put in a link in the chat, too, for anyone who's interested in that. There's some questions about medications. There are always a lot of questions about medications. And because we really don't have time to go into there, I'm going to refer you guys back to the prior episodes. We have full episodes on current drugs. And we're going to be doing more of those, what is Kisunla, what is donanemab. We have a Dementia Drugs Town Hall. And we're going to be doing an episode soon about new drugs for agitation, symptoms of agitation in people with dementias and also on ultrasound opening the blood-brain barrier. It's just for those of you who are interested.

But one of the things I think we have only a few minutes. But, Ron, I want to ask, Lizzie from the UK actually sent this in, "At what stage is it advisable to contact a doctor if you have concerns? What if you are dismissed as being too young or feel you can't push any further?" So we're going to be honest here, we go to our primary care physician who's rushed, and busy, and has seven minutes to say whatever, and they don't really know much about all these things that you know so much about. What can people do to try to get—and even I have a cousin whose husband was just diagnosed with mild cognitive impairment, from a neurologist, which is hard to get an appointment. And when asked what could we do, the neurologist said, come back in a year. Now, that's not great advice because if you try to treat that today, you have a better chance than treating it a year from now. So how can all our friends from all around the country who aren't necessarily really close to the Mayo Clinic, how do they get the best care that they can, let's say?

DR. RONALD C. PETERSEN: In fairness to our primary care colleagues, they are squeezed. As you say, they get 7 minutes, or 15 minutes, or whatever. And the person also has diabetes that may or may not be in control, the hypertension that may or may not be in control, those issues, and say, oh, and in addition, I'm forgetful. I think most primary care people will pay attention to that. And if the primary care person thinks this is a

problem, let's set up another appointment either to see me where we can just delve into that problem or I will refer you out to one of my colleagues who specializes in that. But in the situation where the primary care person is so harried, and has a lot of things to do, and says, ah, you're fine, I'm forgetful, too, which is not uncommon kind of thing, don't necessarily give up on that. You might have another referral source. You might be able to try to get in to see a neurologist, psychiatrist, psychologist, somebody, a geriatrician, who might be able to spend a bit more time with that.

So I think you need to be persistent. And next time you go in to see him or her, you say, this is why I'm here. Yeah, my diabetes is, yeah, yeah, yeah. But I'm here to see you about my memory. Is this something that I need to be concerned about or not? And that may get sufficient attention from the primary care person to deal with it then and/or refer you out. But you have to be mindful of the complex situation that the primary care people are facing and all the demands on them.

NANCY KEACH: And I'm very sympathetic to the primary care physicians, but also, it's very frustrating. I do this 24/7 and have been for 16 years and I still learn something new every day. And so it's completely impossible for a primary care physician to even touch the tip of the iceberg.

DR. RONALD C. PETERSEN: Yep. Nancy, I may expand on one you said, your family member or relative, friend with mild cognitive impairment. Mild cognitive impairment is a diagnosis that's not normal. So just labeling it is probably not sufficient. I think if the primary care person or neurologist has gone far enough to say, I think this is mild cognitive impairment, I think it's incumbent upon the patient to say, yeah, but what's causing it? What is it due to? Don't assume that the mild cognitive impairment is "aging" because it's not. It's an abnormal condition. And don't assume it's early Alzheimer's disease because it may or may not be. So I think it's perfectly reasonable for the patient to ask the neurologist, the physician, OK, you've called it mild cognitive impairment, what's it due to? I have chest pain. Are you just going to stop there? No, you're going to ask me or pursue why I'm having chest pain. So I think that, again, mild cognitive impairment is just the symptom but you want to know what's causing it.

NANCY KEACH: Ron, we have two minutes so I'm going to ask you one last question you can answer in 60 seconds. And thank you so much for coming.

DR. RONALD C. PETERSEN: Oh, my pleasure. Great questions.

NANCY KEACH: Great to have you. And I'm going to ask you to commit to come back a while from now and update us maybe a year from now.

DR. RONALD C. PETERSEN: Happy to.

NANCY KEACH: Micah from New York City asked, "Name one takeaway or action item you would like to impart to this audience."

DR. RONALD C. PETERSEN: Thank you very much, Micah, for that, because I think it's going back to the beginning of the clinical picture, cognitively unimpaired, mild cognitive impairment, dementia, what are they due to. And I think a good closing mindful element of the discussion is that Alzheimer's disease is very important. It's very common. But it may not be the only game in town. It's quite often most people who have cognitive impairment in their 70s or 80s may have amyloid, may have tau, Alzheimer's disease, but they may have some of this alpha-synuclein, that may have some of this TDP-43. They may have some vascular disease. They may have some things called CSF dynamics. It's often multifactorial. Some of the elements are treatable, some of them are not.

But I think down the road, beyond my time, probably, I'm thinking that when people go in to see their primary care physician, they'll get the lipid screen, how's your LDL, your HDL, your triglycerides, and then get your cognitive screen, that's hopefully a blood test that's going to be able to tell you you've got X amount of this protein, that protein, that protein, and most importantly, here's what we do about it because we may have treatments for those. And it's probably going to take combination therapy down the road to treat cognitive disorders. Alzheimer's disease is very important, but it's just a part of that total picture. So I'm optimistic that we're developing new biomarkers for all these different entities which are going to lead to treatments.

NANCY KEACH: Oh, that's great. Thank you for ending on a hopeful note. And thank you so much for sharing your expertise with us. Really appreciate it.

DR. RONALD C. PETERSEN: My pleasure, Nancy. Thanks for having me.

NANCY KEACH: Thanks, Ron. And let's see, let's just put up the last couple of screens here. If you would like some free resources about Alzheimer's disease, here are free print publications we can send to you or send you a PDF. Let's go to the next slide. If you have suggestions for future topics, please email us at reply@brightfocus.org.

On Thursday, May 15, we have "How Focused Ultrasound is Changing Alzheimer's Treatment" with Dr. Ali Rezai. I think that's going to be a fantastic and interesting episode. There's a lot happening in ultrasound. And we thank you so much for coming.

The program is no fun if nobody comes. So thank you so much for coming and gaining from these wonderful experts. We look forward to seeing you next month. Be well, hug the person that you love, and have a great rest of the week.

Resources:

- BrightFocus Article: Environmental Pollution Can Increase Your Alzheimer's Risk, Say BrightFocus-Funded Scientists