Biomarkers for Alzheimer's Diagnosis? - Frankly Speaking EP 69

Transcript Details

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Dr. Frank Domino:

You're finishing your visit with Mariel following up her hypertension and hyperlipidemia. She mentions her father who she believes is developing dementia and wants to know if he should get one of those new blood tests to see if he really is developing a problem. What do you do and how do you counsel Mary? Hi, this is Frank Domino. And joining me today on the show is Robert Baldor, Professor and Senior Vice Chair in the Department of Family Medicine in Community Health at the University of Massachusetts Medical School and Editor of Baldor's Family Medicine Board Review book. Welcome to the show, Bob.

Robert A. Baldor, MD, FAAFP:

Thanks, Frank. Great to be back.

Dr. Frank Domino:

Great, great to have you. So there's new guidelines regarding the diagnosis of dementia and in particular Alzheimer's disease. Can you help us understand what's changed and what's the current state of affairs?

Robert A. Baldor, MD, FAAFP:

Yeah, this is fascinating. We're gonna be hearing a lot more of this in the news here recently as this has just come out. And basically it's a new classification system. Prior to this time, Alzheimer's has really been a diagnosis made on neurocognitive testing. And what you're saying is, "You know what? We're beginning to refine biomarkers." We have biomarkers that are really helping us to understand Alzheimer's disease, and we should be using biomarkers to really work with the diagnosis of this. Although I will tell you, this is primarily in the research realm at this point to sort of say who are we looking at who has dementia, who has Alzheimer's. And we know that a number of drugs have been shown to not be effective. And so, what this guideline and the classification system is doing is saying, can we detect people with changes with these biomarkers earlier on before they become demented and we're not seeing a benefit, and if we also see subgroups of patients so we can have more targeted pharmacologic therapies for this.

Probably 30% of individuals with Alzheimer's in these studies don't have amyloid. Naturally the anti-amyloid drugs aren't going to work. So how do we screen those people out? That's a little bit what this is getting at, is trying to have a little more defined system of being accurate and being clear when we have somebody in a research protocol that has Alzheimer's, they truly have Alzheimer's, they don't just have some other dementia. That's really what this is really gonna be helpful for.

Dr. Frank Domino:

Well, so it sounds like we're moving away from our former approach where we do neuropsych testing, and we put them through a battery of other screening tests and verbal interactions to make a very subjective diagnosis, to one that's considerably more objective. But, biomarkers, is this something that I as a family physician should be ordering when I suspect people have some dementia onsetting... Having some onset of dementia

symptoms?

Robert A. Baldor, MD, FAAFP:

Well, maybe we should draw a little blood on you today and see. We could start that, but a little bit of this is that... I wanna back you up a little bit. And we're not moving away from neurocognitive testing by any means. That's still there, they're still used in the clinical realm. And really the focus of this will be for research. And they're talking about three particular biomarkers. Amyloid we've known about for a long time. Amyloid is a protein that's been found in the brain and you get these clumps of amyloid in the brain in individuals with Alzheimer's. And this clumping interferes with neuro functions so that the neurons aren't working as well. The second one is something called tau. And these are also proteins. Now, tau proteins are found primarily in the central nervous system, and they're responsible for stabilizing the micro tubules, a functioning of those neuro brain cells so that they function better. And these too are in Alzheimer's dysfunctional and begin to clump up as well.

The third biomarker they talk about is neurodegenerative changes that are seen. If you look at these, these can be assessed not by blood test. They use CSF fluids. You get a spinal tap and you're assessing levels of amyloid in the CSF or tau proteins in the CSF. You can also do PET scanning to detect these. And interestingly enough in Europe, there's much more of a use for CSF in doing spinal taps. In the United States we're more likely to do PET scanning looking for this. But there are currently no FDA-approved clear guidelines or mechanisms for doing tau screen for PET scanning. It's being done right now in research arenas. The third biomarker is this neurodegeneration that you're seeing, and this can also be looked at by looking at CSF levels of total tau. Usually, this is by PET scanning or by MRI scanning looking for brain atrophy. So that's really what we're looking at here is this concept of, can we earlier on detect some of these changes before we're dealing with dementia and have that.

Dr. Frank Domino:

Alright, so, Mary, let's say Mary brings her dad in tomorrow. What approach should we have? What should we be doing in the office and what should we advise her going forward?

Robert A. Baldor, MD, FAAFP:

Yeah. For the most part, we're going to do the same advice we've had right along. And I think it's... If she has a considerable concern, probably it's reasonable to do some neurocognitive testing to see, does he have mild cognitive impairment or more severe symptomatology? And then thinking about what are the therapies we're going to be using for that. And I think we talked about that in prior sessions as to what could be done in that realm. What this new classification does, it's really targeted for looking at people with more pre-clinical disease or mild cognitive impairment that are on the path to developing Alzheimer's. If you think about these classifications they're talking about with these biomarkers, you have amyloid, tau and neurodegeneration, you can actually assess a patient and come up with a schema for them. Somebody could be amyloid negative, if you're amyloid negative you probably don't have Alzheimer's even if you have dementia.

That's really beginning to look at how do we test that... Screen those people out of those research studies so we're not trying to do research on 'em. But you could be amyloid negative and tau positive, but neurodegeneration negative. Well, that's probably more of a pre-clinical stage. Can we pick people up that have just amyloid or just tau earlier on, before they're actually exhibiting signs of mild cognitive impairment or dementia, and that's when the research should really impact on looking at agents that are gonna help us prevent that progression. This is really exciting. I think the problem, though, is as it gets out there people are gonna come in and say, "Well, can we get the amyloid test? Can I get that

PET scan done?" They're not gonna come in asking for a spinal tap, I can reassure you...

Dr. Frank Domino:

I would guess not.

Robert A. Baldor, MD, FAAFP:

But the PET scanning is... And so for amyloid it's out there, for tau it's still more research labs. You're probably gonna have trouble getting prior authorization to get the scanning done, 'cause it's still in the realm of experimental therapy. But I think that over the next three years we'll be doing more and more of these tests on people with suspicion. Really what you would do, in my mind, would be somebody of positive family history or earlier on beginning to show signs of mild cognitive impairment. Let's look at them a little more closely and start doing some of these, whether it's PET scanning or spinal fluid analysis, and trying to get the... Today, no. Three years from now, I bet we'll be at that point. And five years from now we'll have that blood test that'll be out there to be able to detect remnants of these things in the blood. That's my prediction, and you'll have to have me back in five years to talk about the blood.

Dr. Frank Domino:

That sounds like a plan, Bob. I just wanna remind everyone that in the meantime, we should be looking for reversible causes of mild cognitive impairment. So when you suspect this, consider thyroid, consider a sleep study and the other things that we have in our differential diagnosis.

Robert A. Baldor, MD, FAAFP:

And I'm gonna put on there drugs, look at what medications they're on, because there's a lot of medications that... And also alcohol, but medications that really interfere with

executive functioning and... So, look at that too as well.

Dr. Frank Domino:

Well, thanks so much, Bob. This is wonderful. It's really quite interesting, and I bet you're right. I bet within the next three to five years, we'll be ordering tests for patients with mild cognitive dysfunction to identify early onset dementia and treat it aggressively. Thanks again.

Robert A. Baldor, MD, FAAFP:

Great, thank you, Frank.

Dr. Frank Domino:

Practice Pointer. New tests are available to help identify dementia in its very early stage. These are primarily used for research, but anticipate knowing more about them over the next three to five years as they'll become much more apparent in our practice. Join us next time when we discuss new data on how we should approach adverse symptoms of the perimenopausal period.