SPEAKER: If I wondered if a patient might have Fabry Disease, one of the next questions then is, well, how do I find out? How do I get to the final answer that I need?

There are two ways to do it. Traditionally the-- in men, the way to establish the diagnosis of Fabry Disease has been to measure the enzyme activity for alpha-galactosidase A. And it's very reliable in men and can confirm the diagnosis. You get a level of less than 20% of the expected, then that man is likely to at some point in his life develop symptoms of Fabry Disease. And if the level is measured at less than 1% of expected activity, then the male patient is very likely to have classical and severe Fabry Disease.

The challenge with the enzyme activity is that it's not very reliable for women, because in women, due to X-inactivation, they will have some cells in their body that make the enzyme. So if you measure the enzyme level, you will pick up often a normal enzyme level or only slightly decreased. And that doesn't correlate well with symptoms.

One might wonder if the women's bodies do make enzyme, how did they become symptomatic? And we'll have to talk about that later. But for women to confirm a diagnosis of Fabry Disease, the gold standard is to sequence the gene and look for a mutation.

That approach can also be used as the first-line approach for men with Fabry Disease, although honestly, I think you should measure-- in men, you should measure both the enzyme activity and sequence the gene when you're trying to confirm the diagnosis. In women, I like to get the enzyme activity. But it's not very helpful in predicting symptomatology or even classifying which type of Fabry Disease the woman will have.

The specific mutations when they are identified, we try to categorize them into classical, which means usually less than 1% of enzyme activity in the males. And it's a very severe deficiency. And that has childhood onset with presenting symptoms of pain, GI symptoms with progression to kidney disease, heart disease, and increased risk for stroke.

And nonclassical disease, which has later onset of symptoms typically in adolescence or adulthood for both men and women and often will lack some of the symptoms. So for example, with the nonclassical Fabry Disease, you will have less risk for GI symptoms and pain, also often less risk for kidney disease. But heart disease becomes the predominant symptom for that form. So it's important to not only know that you have Fabry Disease, but also which form of Fabry Disease-- is it classical or nonclassical?