**SPEAKER:** Fabry disease is a lifelong disease, and since its first discovery back in the 1890s, it has been recognized that it can have onset of symptoms in childhood. However, most of the management and research on Fabry disease has focused on adult symptoms because they are more serious.

First storage starts in the prenatal period. First symptoms, average age for boys with Fabry disease is around 5 to 6 years of age. If you ask families who have a child with Fabry disease. If you ask adults to remember back to when they first had symptoms, they typically report 9 to 12 years of age for boys.

For girls, it's a little bit later with the families who have children reporting first symptoms around age 9. The adult women who are thinking back on their childhood will typically report first symptoms around age 12 to 14.

We actually did a study a few years ago-- Don Laney was the lead author-- and the question for that was what are the first recognizable signs or symptoms of Fabry disease, and we found clearly reported cases with symptom onset as early as 2 years of age. Now, at that age, obviously, the descriptions from the patients are limited, but we found evidence of acroparethesias, which is neuropathic pain primarily involving the hands and feet, as well as GI symptoms in that age range. You can also see very early onset of abnormal sweating. Most frequently, that would be decreased or absent sweating, but occasionally, particularly in females, you'll see excessive sweating as well.

The initial presentation of pain is often during acute illnesses, so with a fever or with other symptoms of an acute infection. And then as the disease progresses, the pain increases in frequency. Other triggers of pain besides acute illnesses can be increased-- exercise, hot or cold weather-- and sometimes, we'll see episodes of pain without an obvious trigger.

There is a significant difference in the way the pain is described between men and women. Both men and women will report a baseline level of pain that is a burning or tingling feeling in the hands and feet. It's usually of moderate severity. But men will have episodes more frequently of what they refer to as crisis pain. Just pain that's severe enough to be debilitating and that they can't function that during the time that they're experiencing it. That happens less frequently but can is obviously quite important in a quality of life standpoint.

There is no obvious physical sign of the pain. So you look at the patient, they appear healthy, they don't usually have swelling or redness or joint limitations. They just report pain, but the pain is severe enough that people will not walk when they are feeling particularly severe pain.

The GI symptoms will also be quite variable with episodes of abdominal pain with or without diarrhea. And sometimes diarrhea will occur without abdominal pain. The diarrhea is intermittent and variable. Some people report that they get most of their GI symptoms when they have high fat or spicy foods. Other people will report that there is no correlation with what they're eating or what they're doing.

The GI symptoms can be quite significant. We've had a number of patients who report that they will-- when they go out to restaurants, they will only order drinks and order their food to go because they aren't sure that they can get to the restroom quickly enough. Or will, sometimes, just make sure that they sit-in the restaurant close to the restroom.

I had one patient who described to me the seriousness of his GI upset with, well, I can't work because who's going to pay you when you spend five or six hours in the bathroom each day? So this is not sort of a mild GI disturbance.

On the other hand, it can be difficult to distinguish the GI disease and Fabry disease from abdominal pain of other causes. GI distress is quite common in the general population affecting up to 25%. So the 40% to 50% of patients with Fabry disease that might report GI symptoms is not necessarily all distinct from the general population. So that makes using the GI symptoms as a presentation a little bit tricky for knowing when to consider testing for Fabry disease.