SPEAKER 1: In females, due to the random X chromosome inactivation, they may have Fabry disease. They may even have Fabry-related kidney injury. And I forgot to say this activity may be normal.

So if you have a very high suspicion of Fabry disease in females, you should move to the second diagnostic step. And this second diagnostic step you do after finding low alpha-galactosidase A activity in a male-- or with a very high suspicion of Fabry in a female even if-- alpha-galactosidase A activity is normal.

The second step is a screening for the mutation. So sequencing the a-Gal A gene, the G-A-L-A gene. And you should find there a pathogenic a-Gal A mutation which underlies the low enzymatic activity.

Sometimes you'll find a genetic valiant in the a-Gal A gene that is of unknown significance. So you cannot really be sure whether the patient has or does not have Fabry disease because the genetic variant has not been characterized.

So here you have our third diagnostic test that, if it's available, you maybe do also together with the genetic testing, which is assessing for the circulating levels of lyso-Gb3. Lyso-Gb3 is metabolite that is circulating in huge amounts in Fabry patients. And it's virtually absent-- very, very low levels-- in healthy controls.

So if the patient has Fabry disease, natural Gb3 levels should be high. And normal lyso-Gb3 levels are usually interpreted as excluding Fabry disease in males.