



UNEXPLAINED NEUROLOGIC SYMPTOMS COULD HELP IDENTIFY A FABRY FAMILY

Fabry Disease:
A Quick Reference for Neurologists

CLINICAL DIAGNOSIS



About Fabry Disease

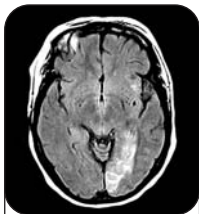
Fabry disease is a genetic disorder caused by deficiency of α -galactosidase A enzyme activity, resulting in an inability to catabolize certain lipids, particularly globotriaosylceramide (GL-3). GL-3 progressively accumulates in the vascular endothelium and tissues, including visceral tissue, throughout the body.

Neurologic manifestations:

- Pain in the extremities (acroparesthesia)
- Hypohidrosis/anhidrosis
- Heat/cold & exercise intolerance
- Vertigo
- Diplopia
- Vascular brainstem dysfunction
- Progressive cerebral vasculopathy
- Large and small vessel vascular disease
- Premature stroke
- Progressive white matter lesions
- Altered cerebral blood flow

Other manifestations:

- Angiokeratomas (dilated dermal vessels)
- Gastrointestinal complications
- Corneal and lenticular opacities
- Renal insufficiency
- Cardiac dysfunction



White matter lesions on MRI, demonstrating evidence of cerebrovascular infarct.

CLINICAL DIAGNOSIS

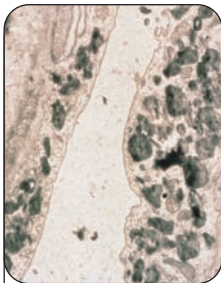
CONFIRMING DIAGNOSIS



Neurologists may be the first to identify Fabry disease. In patients with neurologic symptoms and a family history of early cerebrovascular, cardiac, or renal disease, diagnostic testing can determine whether Fabry disease is the underlying cause.

Diagnostic Tests

- Diagnosis in males and females can be made by testing for deficiency of α -galactosidase (α -GAL) enzyme activity in plasma, leukocytes, tears, or dried blood spots. In females, however, normal α -GAL enzyme activity does not rule out Fabry disease, and genetic analysis must also be conducted.
- For assistance in locating a facility that performs genetic analysis, please contact Genzyme Medical Information at **800-745-4447** (option 2) or **617-768-9000** (option 2).



Progressive accumulation of substrate in the vascular endothelium leads to ischemia and infarction of these vessels.

CONFIRMING DIAGNOSIS

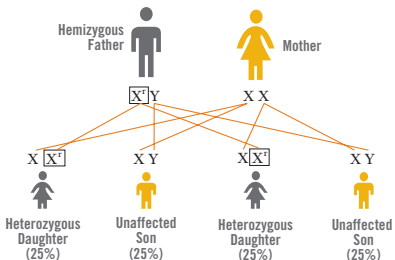
GENETIC IMPACT



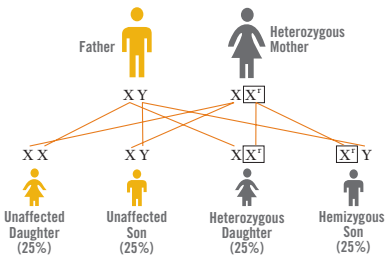
Males with the defective gene pass it on to all of their daughters and none of their sons. Heterozygous females have a fifty percent chance with each pregnancy of passing the defective gene to each of their offspring. Most females heterozygous for Fabry disease are clinically affected to some extent.^{1,2}

Inheritance Pattern

Segregation of X-Linked Trait (Hemizygous Father)



Segregation of X-Linked Trait (Heterozygous Mother)



GENETIC IMPACT



QUESTIONS TO ASK YOUR PATIENT

If you suspect Fabry disease, consider asking your patient these questions. Affirmative answers could indicate that diagnostic testing is warranted.

Questions for Clinical Assessment

- Do you experience recurrent tingling or burning in your hands or feet?
- Have you ever experienced episodes of extreme pain of unknown cause, possibly accompanied by fever?
- Do you have trouble sweating or exercising?
- Do you find heat or cold hard to tolerate?
- Do you have gastrointestinal problems such as pain and bloating after eating, or nausea, cramps, or diarrhea?
- Do you have frequent and urgent bowel movements?
- Do you have any small raised reddish-purple spots on your skin, especially in the “bathing trunk” area?
- Does anyone in your family have kidney failure of unknown cause?
- Do you or anyone in your family have heart disease that developed at a relatively early age of unknown cause?
- Have you or anyone in your family had a stroke at a relatively early age?

RESOURCES



Genzyme is committed to helping medical professionals get the information and resources they need to provide comprehensive care for their patients with Fabry disease.

Please contact Genzyme for:

- Patient resources and information on advocacy groups to help connect patients and their families to others living with Fabry disease.
- Information regarding diagnostic testing and genetic counseling.
- Fabry disease information and educational resources.
- Information on the Fabry Registry, an international database sponsored by Genzyme to help increase the understanding of Fabry disease.

For more information:

Call **800-745-4447** (option 2) or
617-768-9000 (option 2)

Monday – Friday 8am to 6pm US Eastern Time

Email **fabry@genzyme.com**

Visit **www.genzyme.com**
or **www.fabrycommunity.com**

REFERENCES

1. MacDermot KD, Holmes A, Miners AH. Anderson-Fabry disease: clinical manifestations and impact of disease in a cohort of 60 obligate carrier females. *J Med Genet* 2001;38:769-775.
2. Gupta S, Ries M, Kotsopoulos S, Schiffmann R. The relationship of vascular glycolipid storage to clinical manifestations of Fabry disease: A cross-sectional study of a large cohort of clinically affected heterozygous women. *Medicine* 2005;84:261-268.

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The logo for Genzyme, featuring the word "genzyme" in a lowercase, sans-serif font. The letters are black and have a clean, modern appearance.