Fabry Disease Testing Algorithm*

Fabry disease is an X-linked disorder; males will be symptomatic, carrier females may or may not be symptomatic. Genetic consultation is recommended.

Patients with at least 1 of the following indications*:
- Positive or suspected family history
- Angiokeratomas
- Peripheral neuropathy
- Proteinuria
- Cardiovascular disease
- Or any associated feature

*A separate algorithm is available for positive newborn screen results, see Fabry Disease: Newborn Screen-Positive Follow-up algorithm.

FABRZ / Fabry Disease, Full Gene Analysis (can be performed on specimen received for AGA or AGABS test)
- Fabry disease highly unlikely (<1% of affected males have leukocyte enzyme values within the normal range); consider evaluation for other diseases
- Reduced enzyme result suggests Fabry disease
- Suggests the presence of a mutation that is undetectable by this method
- No mutation
- Mutation detected
- Reduced enzyme activity
- FABRZ / Fabry Disease, Full Gene Analysis (can be performed on specimen received for AGA or AGABS test)
- Confirmed diagnosis of Fabry disease
- Consider performing FMTT / Familial Mutation, Targeted Testing for at-risk family members

AGA / Alpha-Galactosidase, Leukocytes
AGABS / Alpha-Galactosidase, Blood Spot
AGAS / Alpha-Galactosidase, Serum**

Females

Normal enzyme activity
Reduced enzyme activity

Recommended initial evaluation: (select 1)
- AGA / Alpha-Galactosidase, Leukocytes
- AGABS / Alpha-Galactosidase, Blood Spot
- AGAS / Alpha-Galactosidase, Serum**

Due to low sensitivity of enzyme testing for females, the following evaluations are also recommended:
- CTSA / Ceramide Trihexosides and Sulfatides, Urine
- Ophthalmology exam with slit-lamp
- Cardiac evaluation for Fabry disease
- Renal evaluation for Fabry disease

Any abnormal finding
No abnormal finding

Consider evaluation for other diseases

If proband is available, determine family mutation by testing proband first
If proband is not available, perform FABRZ / Fabry Disease, Full Gene Analysis on the female patient

NO

YES

Males

Positive family history with mutation identified

FMTT / Familial Mutation, Targeted Testing

NO

Females

Recommended initial evaluation (select 1)
- AGA / Alpha-Galactosidase, Leukocytes
- AGABS / Alpha-Galactosidase, Blood Spot

Mutation detected

Mutation detected

Suggests either:
- Other diseases
- Presence of a mutation that is undetectable by this method

Consider evaluation for other diseases

NO

YES

Mutation detected

No mutation

Confirmation of Fabry disease

*An interpretive report is provided for all tests in this algorithm.
**Molecular genetic testing cannot be added to this specimen type and would require a new specimen collection.