Discover Fabry Disease:

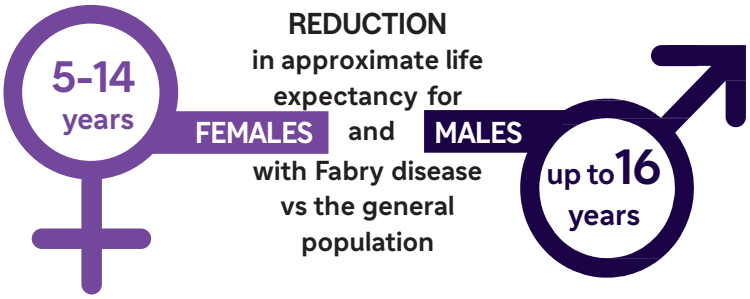
THE ROLE OF THE NEPHROLOGIST

KIDNEY MANIFESTATIONS OF FABRY DISEASE ARE COMMON AND CAN BE LIFE THREATENING.[1,2]

Fabry disease is a rare, progressive, and potentially life-threatening disorder that starts in early childhood and affects men and women.[2-4]

As an X-linked lysosomal storage disorder that is multisystemic, Fabry disease is caused by complete or partial deficiency of the lysosomal enzyme α-GAL A, leading to GL-3* and lyso-GL-3** accumulation that can result in damage to the kidneys, heart, and cerebrovascular system.[4]

EARLY DIAGNOSIS AND MANAGEMENT ARE CRITICAL AS FABRY DISEASE CAN DECREASE LIFE EXPECTANCY DUE TO ORGAN DAMAGE.[4-7]



REDUCTION in approximate life expectancy for FEMALES and MALES with Fabry disease vs the general population

THE PREVALENCE OF FABRY DISEASE IN THE DIALYSIS POPULATION IS HIGHER THAN IN THE GENERAL POPULATION.[8-12]

10x - 108x higher in FEMALES[8-10,†]

80x - 480x higher in MALES[8,11,12,‡]

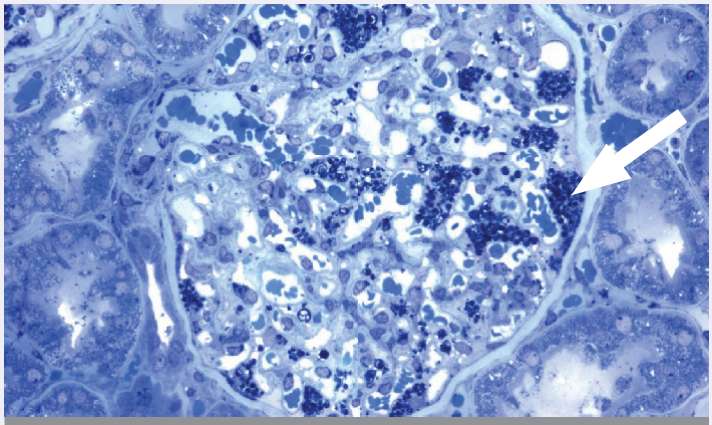
IDENTIFY MULTI-SYSTEM INVOLVEMENT IN CLASSIC FABRY DISEASE

Patients may experience a myriad of symptoms, including:

- Microalbuminuria, Proteinuria[1,2]
- Podocyte injury (can occur in the absence of albuminuria)[1,2,13]
- Elevated serum creatinine[1,2]
- Glomerular sclerosis[1,2]
- Fibrosis[1,2]
- Progressive renal insufficiency[1,2]
- ESKD[1,2]
- Progressive LVH, angina, myocardial fibrosis, and arrhythmias[3,14]
- Early ischemic stroke[3,14]
- Peripheral neuropathy of extremities/ episodic pain crisis beginning in childhood[14]
- Hypohydrosis[14]
- GI manifestations: diarrhea, abdominal pain[14]
- Angiokeratomas[14]

KIDNEY SYMPTOMS OF FABRY DISEASE CAN BE CONFUSED WITH

- Diabetes mellitus, arterial hypertension, or systemic lupus erythematosus[15]
- Chronic glomerulonephritis[2]
- Familial Mediterranean fever and secondary amyloidosis[16]



Kidney biopsy (light microscopy): the purple stain is on the podocytes where there is the most prominent collection of GL-3 in the kidney. Reprinted with permission from *Orphanet J Rare Dis.* Germain DP. 2010;5:30.

*GL-3 and Gb3 are interchangeable terms for globotriaosylceramide.
**lyso-GL-3 and lyso-GB-3 are interchangeable terms for globotriaosylsphingosine.
†Prevalence of Fabry disease in females: 1 in 20,000. Prevalence of Fabry disease in females on hemodialysis: 0.05% to 0.54% (10x to 108x-fold).[8-10]
‡Prevalence of Fabry disease in males: 1 in 40,000. Prevalence of Fabry disease in males on hemodialysis: 0.2% to 1.2% (80x to 480x-fold).[11,12,17]

α-GAL A, α-galactosidase A; ESKD, end-stage kidney disease; GL-3, globotriaosylceramide; LVH, left ventricular hypertrophy; lyso-GL-3, globotriaosylsphingosine.

KIDNEY INVOLVEMENT MAY WARRANT FABRY DISEASE SCREENING[18]

CONSIDER FABRY DISEASE IN YOUR DIFFERENTIAL DIAGNOSIS WHEN[15]:

Presentation
Microalbuminuria, proteinuria, reduced GFR, hematuria (rare), renal cysts (mainly parapelvic), and (in early disease) reduced systemic BP and glomerular hyperfiltration[19]

Family History
Cardiomyopathy, arrhythmias, premature stroke, sudden cardiac death, and kidney failure[20,21]

Laboratory and Biopsy Findings
Urinalysis: "Maltese cross" and "urinary mulberry cells"
Biopsy: Glomerulosclerosis, vascular lesions, vacuolation, and lysosomal GL3 deposits[19]
Biochemical: Fabry specific biomarkers: GL-3 and Lyso-GL-3

Rule out Fabry disease in your patients with unexplained CKD.

	SCREENING RECOMMENDATIONS[22]	TESTING IS STRAIGHTFORWARD[14,23]
Males	Screening **MALES** <50 years of age with unexplained CKD	**α-GAL A enzyme assay** and/or ***GLA* gene sequencing**
Females	Screening **FEMALES** at any age with unexplained CKD and other symptoms associated with Fabry disease	***GLA* gene sequencing** Affected females may have normal-to-low enzyme activity in plasma or leukocytes; therefore, *GLA* gene sequencing is required to confirm diagnosis in females.

Damage to kidney, cardiac, and cerebrovascular systems can have a life-threatening impact. Monitor patients in accordance with published management guidelines and clinicians' medical expertise.[14]

Suspect Fabry disease? Test as soon as possible.

*GL-3 and Gb3 are interchangeable terms for globotriaosylceramide. Fabry-specific biomarkers GL-3 and lyso-GL-3 are elevated in urine and plasma in males. Plasma GL3 can be normal in affected females.

BP, blood pressure; CKD, chronic kidney disease; GFR, glomerular filtration rate; *GLA*, galactosidase-alfa.

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MAT-US-2203431-v3.0-08/2026

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