**Fabry Disease**

Fabry Disease is one of the lysosomal storage disorders. It is caused by a defect in the alpha-galactosidase A (GLA) gene. The enzyme GLA breaks down globotriaosylceramide (GL3) that is made from galactose and lactose in the lysosome. If not broken down, GL3 cannot leave the lysosome resulting in deposits of glycosylsphingolipids in tissues throughout the body, especially in the kidney, heart and brain. There is a wide variability in severity and age of onset in both males and females. Infants are typically asymptomatic.

Forms:

* Classic form of Fabry
  + Occurs in males with <1% alpha-Gal A activities.
  + Symptoms usually appear in childhood or adolescence:
    - Episodes of pain in hands and feet (acroparesthesias)
    - Clusters of small, dark red spots on the skin (angiokeratomas)
    - Decreased ability to sweat
    - corneal opacity
    - hearing loss
  + Over time, more serious complications include:
    - Kidney damage and kidney failure
    - Hypertension
    - Cardiomyopathy
    - Cerebrovascular disease
* Males with residual alpha-Gal A activity may present with either a cardiac or renal form of Fabry later in life
* Females can have clinical presentations ranging from asymptomatic to severely affected.

Incidence: It is estimated that one in every 40,000 male births worldwide is born with classic Fabry; however, an exact rate of occurrence cannot be determined until more states are screening newborns for the disease

Diagnosis: Diagnosis is made by confirmatory testing conducted by or through consultation with an experienced metabolic geneticist.

Confirmatory Tests include:

* Quantitative GLA level –if low, diagnostic in males
* Both GLA level & DNA should be done on all females

Treatment: Enzyme Replacement Therapy (ERT) may reduce the long-term risk for cardiac, cerebrovascular and kidney complications. ERT is available for both males and affect females. Pain management and kidney support may also be needed. Individuals with Fabry Disease should be followed yearly and have a MRI every 2 years.

False Positives: Low GLA can be found in pseudodeficiencies which can be detected through newborn screening.