MAYO CLINIC LABORATORIES

Newborn Screening Act Sheet

Guanidinoacetate Methyltransferase Deficiency: Increased Guanidinoacetate

Condition Description: Guanidinoacetate methyltransferase (GAMT) deficiency is a disorder of creatine synthesis caused by a deficiency of the enzyme, GAMT, resulting in brain creatine deficiency and neurological symptoms such as seizures, developmental delay, behavioral problems, and abnormal movements. Onset varies from early infancy to childhood. GAMT is an autosomal recessive condition.

You should take the following actions:

- Contact family to inform them of the newborn screening result and ascertain clinical status (hypotonia, epilepsy). Clinical signs may not be present in newborns with confirmed GAMT deficiency.
- Consult with genetic or metabolic specialist.
- Evaluate the newborn. If any neurologic symptom is present or infant is ill, transport to hospital for further evaluation and treatment in consultation with metabolic specialist.
- Initiate timely confirmatory/diagnostic testing and management, as recommended by specialist.
- Provide family with basic information about GAMT deficiency.

Diagnostic Evaluation: Confirmatory testing should include measurement of guanidinoacetate (GAA), creatine, and creatinine in both urine and plasma. Patients with elevated values of GAA and decreased levels of creatine in the urine and plasma may require *GAMT* gene analysis in consultation with the pediatric metabolic specialist.

Clinical Expectations: Individuals with GAMT deficiency primarily present with neurologic symptoms ranging from early infancy (3-6 months) to early childhood. The typical manifestations are intellectual disability and epilepsy, but patients may also have global developmental delays, significant behavioral disturbances (such as self-mutilation) and abnormal movements. Treatment consists of supplementation with creatine monohydrate to increase cerebral creatine levels as well as ornithine supplementation and dietary protein restriction to decrease cerebral GAA levels. Individuals with GAMT who are treated before the appearance of symptoms may exhibit normal neurodevelopmental outcomes. Treatment must be continuous and lifelong to ensure long-term benefit. GAMT deficiency is caused by mutations in the *GAMT* gene and is rare, with less than 150 patients reported.

Additional Information

Genetics Home Reference

Genetic Testing Registry

Mayo Clinic Laboratories Testing

CRDPU / Creatine Disorders Panel, Urine