Maryland
DEPARTMENT OF HEALTH
Wes Moore, Governor · Aruna Miller, Lt. Governor · Laura Herrera Scott, M.D., M.P.H., Secretary

Laboratories Administration
Robert A. Myers, Ph.D., Director
1770 Ashland Avenue
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MEMORANDUM

Date: December 2, 2024

To: All providers of Newborn Screening specimens

From: M. Christine Dorley Ph.D. mcD
Chief Newborn Screening Division, Laboratories Administration

Through: Robert A. Myers, Ph.D. RAM
Director, Laboratories Administration

Subject: Newborn Screening for GAMT deficiency

We are pleased to announce that beginning December 2, 2024, the Maryland Department of Health (MDH) Newborn Screening (NBS) Laboratory will begin screening all babies born in Maryland for guanidinoacetate methyltransferase deficiency (GAMT) as part of the routine NBS panel.

For questions or inquiries regarding GAMT screening, please contact the MDH NBS Laboratory at 443-681-3900 or by email at mdphl.nbs@maryland.gov . For inquiries about the interpretation of results please contact the MDH NBS Follow-up Unit at 443-681-3916 or by email at: mdh.newbornscreeningfollowup@maryland.gov .

Attached is a brief description of the disorder.

Cc: Dr. Kalyanaraman
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Laportia Barrows
Erin Penniston

Guanidinoacetate Methyltransferase Deficiency

What is Guanidinoacetate methyltransferase (GAMT) deficiency? Guanidinoacetate methyltransferase (GAMT) is an autosomal recessive inherited disorder caused by a deficiency in creatine (CRE) which is essential for energy production and storage. The GAMT gene encodes the enzyme responsible for CRE production from a compound called guanidinoacetate (GUAC). Pathogenic variants in the GAMT gene result in a deficiency or defective GAMT enzyme and subsequent buildup of GUAC which is toxic to the brain and muscles. So far, 15 pathogenic gene variants have been identified to cause GAMT deficiency.

What are the signs and symptoms of GAMT deficiency? Signs and symptoms vary and can include development delays, seizures/epilepsy, progressive movement disorder, muscle weakness, intellectual disability, and behavior disorders. Infants and toddlers with GAMT deficiency can be misdiagnosed as cerebral palsy. Older children with GAMT deficiency are misdiagnosed as autism or global developmental delay.

How does GAMT deficiency progress? The onset of GAMT is variable beginning from three months of age up to three years of age. Carriers of a pathogenic GAMT variant do not have or will not develop disease. A person with GAMT deficiency can live as long as a person with the deficiency.

What is the epidemiology of GAMT deficiency? GAMT deficiency is a rare disorder first described in 1994 with about 120 affected individuals worldwide reported in the literature with most being of Portuguese ancestry. The reported birth prevalence is 1/550,000 to 1/250,000.

Can GAMT deficiency be treated? There is no cure but YES, GAMT deficiency can be treated. CRE supplementation is required to restore cerebral CRE levels and improve neurological outcomes. Ornithine supplementation is also warranted due to an increase in Arginine which is a precursor to GUAC. A diet restricting Arginine may help to lower GUAC. Sodium benzoate can also help to lower GUAC levels.

What is the testing strategy at MDH NBS Laboratory? MDH NBS Laboratory will test the dried blood spot specimen for GUAC and CRE. CRE will be used to calculate a GUAC/CRE ratio. A combined elevation of GUAC and GUAC/CRE ratio is considered outside of normal limits. Further follow-up and diagnostic testing which includes urine GUAC and GAMT gene sequencing may be required by a specialist.

Where can more information be found about GAMT? See the following links:

1. Association of Public Health Laboratories: https://www.aphl.org/aboutAPHL/publications/Documents/NBS-NewSTEPs-GAMT-Toolkit.pdf
2. National Organization of Rare Disease (NORD): https://rarediseases.org/rare-diseases/guanidinoacetate-methyltransferase-deficiency/
3. National Institutes of Health: https://rarediseases.info.nih.gov/diseases/2578/guanidinoacetate-methyltransferase-deficiency
4. Health Resources and Services Administration (HRSA): https://newbornscreening.hrsa.gov/conditions/guanidinoacetate-methyltransferase-deficiency