Creatine Disorders Panel Testing

Last Literature Review: January 2022 Last Update: June 2024

Creatine deficiency syndromes include guanidinoacetate methyltransferase (GAMT) deficiency, L-arginine:glycine amidinotransferase (AGAT) deficiency, and creatine transporter deficiency. GAMT deficiency and AGAT deficiency are related to creatine biosynthesis, while creatine transporter deficiency is related to creatine transport. All three disorders are characterized by intellectual disability, seizure disorder (variable severity), developmental delay, speech/language delay, movement disorder, and behavioral disorder (autism, hyperactivity, self-injury). Disease onset is generally observed in early childhood. Diagnosis often includes magnetic resonance (MR) spectroscopy, biochemical testing, and genetic testing. Biochemical testing should include measurement of guanidinoacetate (GAA) and creatine in urine and plasma, and evaluation of the creatine:creatinine ratio in urine.

Featured ARUP Testing

Creatine Disorders Panel, Urine 2002333

Method: Liquid Chromatography-Tandem Mass Spectrometry

Creatine Disorders Panel, Serum or Plasma 2002328

Method: Liquid Chromatography-Tandem Mass Spectrometry

- Initial tests to diagnose or rule out creatine deficiency syndromes following clinical presentation
- Urine and serum/plasma testing should be ordered simultaneously for proper result interpretation

Disease Information

Creatine deficiency syndromes are relatively rare and associated with genetic variance in the *GATM*, *GAMT*, and *SLC6A8* genes. The table below details gene associations, inheritance patterns, and incidence for AGAT, GAMT, and creatine transporter deficiency syndromes.

Disorder	Gene	Inheritance	Incidence
AGAT deficiency	*GATM*	AR	<15 cases known
GAMT deficiency	*GAMT*	AR	1/274,000 in Utah[a] 1/537,000 in New York[a]
Creatine transporter deficiency	*SLC6A8*	XL	>100 cases

[a]Estimated.[1]

AR, autosomal recessive; XL, X-linked

Results

The table below details the expected biochemical results for AGAT, GAMT, and creatine transporter deficiency syndromes. Clinical correlation is necessary for complete evaluation of laboratory results.

Disorder	Plasma/Serum GAA and Creatine	Urine Creatine:Creatinine Ratio
AGAT deficiency	↓ GAA ↓ Creatine	Normal
GAMT deficiency	↑ GAA ↓ Creatine	Normal
Creatine transporter deficiency	Normal	↑ Creatine:creatinine ratio

In addition to GAMT deficiency, elevated GAA can be observed secondary to dietary supplements or in other conditions such as urea cycle disorders. Reevaluation of plasma creatine and guanidinoacetate, and evaluation of plasma amino acid should be performed to exclude a disorder of creatine biosynthesis.

References

1. Hart K, Rohrwasser A, Wallis H, et al. Prospective identification by neonatal screening of patients with guanidinoacetate methyltransferase deficiency. *Mol Genet Metab*. 2021;134(1-2):60-64.

Additional Resources

Ingoglia F, Chong JL, Pasquali M, et al. Creatine metabolism in patients with urea cycle disorders. *Mol Genet Metab Rep*. 2021;29:100791.

Mercimek-Andrews S, Salomons GS. Creatine deficiency syndromes. In: Adam MP, Ardinger HH, Pagon RA, et al, eds. *GeneReviews*. University of Washington, Seattle. Accessed Jan 2022.

Related Information

Cardiovascular Genetic Testing - Hereditary Heart and Vascular Disease
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