Test Definition: CRDPU

Creatine Disorders Panel, Random, Urine

Overview

Useful For

Evaluating patients with a clinical suspicion of arginine:glycine amidinotransferase deficiency, guanidinoacetate methyltransferase deficiency, and creatine transporter deficiency

Genetics Test Information

Depletion of cerebral creatine occurs in all 3 types of creatine deficiency syndromes (CDS): arginine:glycine amidinotransferase deficiency, guanidinoacetate methyltransferase deficiency, and creatine transporter deficiency.

Measurement of guanidinoacetate, creatine (Cr), and creatinine (Crn) in urine, along with the Cr:Crn ratio, aids in distinguishing the types of creatine deficiency syndromes.

Treatment with oral creatine supplementation is effective in some types of CDS.

Creatine supplementation may impact reliability of test results.

Additional Tests

Test Id	Reporting Name	Available Separately	Always Performed
CRBO	Creatine, (Bill Only), U	No	Yes
CRNBO	Creatinine, (Bill Only), U	No	Yes
GAABO	Guanidinoacetate, (Bill Only), U	No	Yes

Testing Algorithm

This is a single test that carries the results for the panel. When the test has been resulted, the following procedures are billed:
-CRBO / Creatine, Urine (Bill Only)
-CRNBO / Creatinine, Urine (Bill Only)
-GAABO / Guanidinoacetate, Urine (Bill Only)

For more information see:
-Newborn Screen Follow-up for Guanidinoacetate Methyltransferase Deficiency (GAMT)
-Epilepsy: Unexplained Refractory and/or Familial Testing Algorithm

If the patient has abnormal newborn screening results for guanidinoacetate methyltransferase deficiency, refer to the appropriate ACMG Newborn Screening ACT Sheet.(1)

Special Instructions

- Newborn Screen Follow-up for Guanidinoacetate Methyltransferase Deficiency
- Epilepsy: Unexplained Refractory and/or Familial Testing Algorithm

Method Name
Liquid Chromatography Tandem Mass Spectometry (LC-MS/MS)

NY State Available
Yes

Specimen

Specimen Type
Urine

Necessary Information
Patient's age and sex are required.

Specimen Required
Supplies: Urine Tubes, 10 mL (T068)
Container/Tube: Plastic, 10 mL urine tube
Specimen Volume: 1 mL
Collection Instructions:
1. Collect a random urine specimen.
2. Immediately freeze urine specimen.
3. If possible, **do not** send other tests ordered on same vial of urine. In doing so, the other tests may have increased turnaround time due to the strict frozen criteria of this assay.

Forms
If not ordering electronically, complete, print, and send a Biochemical Genetics Test Request (T798) with the specimen.

Specimen Minimum Volume
0.5 mL

Reject Due To
All specimens will be evaluated at Mayo Clinic Laboratories for test suitability.

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Urine	Frozen	29 days	

Clinical & Interpretive

Clinical Information
Disorders of creatine synthesis (guanidinoacetate methyltransferase [GAMT] deficiency, L-arginine:glycine

amidinotransferases [AGAT] deficiency, and creatine transporter deficiency [CTD]) are collectively described as creatine deficiency syndromes (CDS). AGAT and GAMT deficiencies are inherited in an autosomal recessive manner, while the creatine transporter defect is X-linked. All 3 disorders result in a depletion of cerebral creatine and typically present with global developmental delays especially expressive speech and language delay and intellectual disability. Affected patients may have abnormal magnetic resonance imaging findings and exhibit cerebral creatine deficiency in brain magnetic resonance spectroscopy. Patients with GAMT and male patients with CTD may develop seizures, autistic-like behaviors, and abnormal movements. Female carriers for CTD can be asymptomatic or exhibit features similar to affected male patients, such as intellectual disability, behavioral problems, and seizures.

Diagnosis is possible by measuring guanidinoacetate (GAA), creatine (Cr), and creatinine (Crn) in plasma and urine. The profiles are specific for each clinical entity. Patients with GAMT deficiency typically exhibit normal to low Cr, very elevated GAA, and low Crn. Patients with AGAT deficiency typically exhibit normal to low Cr, low GAA, and normal to low Crn. In comparison, elevated Cr, normal GAA, normal to low Crn, and an elevated Cr:Crn ratio characterize patients with creatine transporter defect. The only consistently reliable method for diagnosis of CTD in female patients is molecular analysis of the *SLC6A8* gene. The diagnosis of GAMT, AGAT, and CTD can be confirmed by molecular analysis of *GAMT*,*GATM,* and *SLC6A8* respectively.

Treatment with oral supplementation of creatine monohydrate is available and effective for the AGAT and GAMT deficiencies. Patients with GAMT deficiency may also be treated with supplemental ornithine and dietary arginine restriction. CTD is treated with oral creatine monohydrate and arginine and glycine supplementation.

Early treatment has been reported to prevent disease manifestations in affected but presymptomatic newborn siblings of individuals with GAMT or AGAT deficiencies.

Reference Values

Males

Age	Creatinine (nmol/mL)	Guanidinoacetate (nmol/mL)	Creatine (nmol/mL)	Creatine/ creatinine
< or =31 days	430-5,240	9-210	12-2,930	0.02-0.93
32 days-23 months	313-9,040	16-860	18-10,490	0.02-2.49
2-4 years	1,140-12,820	90-1,260	200-9,210	0.04-1.75
5-18 years	1,190-25,270	40-1,190	60-9,530	0.01-0.96
>18 years (male)	3,854-23,340	30-710	7-470	0.00-0.04

Females

Age	Creatinine (nmol/mL)	Guanidinoacetate (nmol/mL)	Creatine (nmol/mL)	Creatine/ creatinine
< or =31 days	430-5,240	9-210	12-2,930	0.02-0.93
32 days-23 months	313-9,040	16-860	18-10,490	0.02-2.49
2-4 years	1,140-12,820	90-1,260	200-9,210	0.04-1.75
5-18 years	1,190-25,270	40-1,190	60-9,530	0.01-0.96
>18 years	1,540-18,050	30-760	5-2810	0.00-0.46

Interpretation

Reports include concentrations of guanidinoacetate, creatine, and creatinine, as well as a calculated creatine:creatinine

ratio. When no significant abnormalities are detected, a simple descriptive interpretation is provided. When abnormal results are detected, a detailed interpretation is given. This interpretation includes an overview of the results and their significance, a correlation to available clinical information, elements of differential diagnosis, and recommendations for additional biochemical testing.

Cautions

Correct specimen collection and handling are crucial to achieve reliable results.

Creatine supplementation will cause falsely elevated results.

Clinical Reference

1. ACMG Newborn Screening ACT Sheets. Accessed December 16, 2024. Available at www.acmg.net/ACMG/Medical-Genetics-Practice-Resources/ACT_Sheets_and_Algorithms/ACMG/Medical-Genetics-Practice-Resources/ACT_Sheets_and_Algorithms.aspx?hkey=9d6bce5a-182e-42a6-84a5-b2d88240c508
2. Clark JF, Cecil KM. Diagnostic methods and recommendations for the cerebral creatine deficiency syndromes. Pediatr Res. 2015;77(3):398-405
3. Mercimek-Mahmutoglu S, Salomons GS. Creatine deficiency syndromes. In: Adam MP, Mirzaa GM, Pagon RA, et al. eds. GeneReviews [Internet]. University of Washington, Seattle; 2009. Updated February 10, 2022. Accessed December 16, 2024. Available at www.ncbi.nlm.nih.gov/books/NBK3794/
4. Stockler S, Schultz PW, Salomons GS. Cerebral creatine deficiency syndromes: clinical aspects, treatment, and pathophysiology. Subcell Biochem. 2007;46:149-166
5. Longo N, Ardon O, Vanzo R, Schwartz E, Pasquali M. Disorders of creatine transport and metabolism. Am J Med Genet. 2011;157:72-78. doi:10.1002/ajmg.c.30292
6. Bahl S, Cordeiro D, MacNeil L, Schulze A, Mercimek-Andrews S. Urine creatine metabolite panel as a screening test in neurodevelopmental disorders. Orphanet J Rare Dis. 2020;15(1):339. doi:10.1186/s13023-020-01617-z
7. Fernandes-Pires G, Braissant O. Current and potential new treatment strategies for creatine deficiency syndromes. Mol Genet Metab. 2022;135(1):15-26. doi:10.1016/j.ymgme.2021.12.005

Performance

Method Description

A random urine sample is combined with stable isotope-labeled internal standards and acetonitrile. After centrifugation, an aliquot of this diluted sample is analyzed by injection onto liquid chromatography columns that separate the analytes from the bulk of the stable isotope dilution in the positive electrospray selected reaction monitoring mode using the Applied Biosystems API 3200 liquid chromatography tandem mass spectrometry system with Analyst software.(Bodamer OA, Bloesch SM, Gregg AR, Stockler-Ipsiroglue S, O'Brien WEO. Analysis of guanidinoacetate and creatine by isotope dilution electroscopy tandem mass spectrometry. Clin Chim Acta. 2001;308:173-178; Cognat S, Cheillan D, Piraud M, Roos B, Jakobs C, Vianey-Saban C. Determination of guanidinoacetate and creatine in urine and plasma by liquid chromatography-tandem mass spectrometry. Clin Chem. 2004;50[8]:1459-1461)

PDF Report

No

Day(s) Performed

Tuesday

Report Available
3 to 9 days

Specimen Retention Time
1 month

Performing Laboratory Location
Mayo Clinic Laboratories - Rochester Main Campus

Fees & Codes

Fees
- Authorized users can sign in to Test Prices for detailed fee information.
- Clients without access to Test Prices can contact Customer Service 24 hours a day, seven days a week.
- Prospective clients should contact their account representative. For assistance, contact Customer Service.

Test Classification
This test was developed and its performance characteristics determined by Mayo Clinic in a manner consistent with CLIA requirements. It has not been cleared or approved by the US Food and Drug Administration.

CPT Code Information
82540
82570
82542

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
CRDPU	Creatine Disorders Panel, U	79290-3

Result ID	Test Result Name	Result LOINC® Value
23383	Creatine	15046-6
23384	Creatinine	14683-7
23385	Guanidinoacetate	97148-1
23268	Creatine/Creatinine Ratio	34275-8
23270	Creatine Disorders Panel Interp	79292-9
23272	Reviewed By	18771-6