Test Definition: HCYSS

Homocysteine, Total, S

Overview

Useful For

An aid for screening patients suspected of having an inherited disorder of methionine metabolism including:

-Cystathionine beta-synthase deficiency (homocystinuria)

-Methylenetetrahydrofolate reductase deficiency (MTHFR) and its thermolabile variants:

-Methionine synthase deficiency

-Cobalamin (Cbl) metabolism

-Combined methyl-Cbl and adenosyl-Cbl deficiencies: Cbl C2, Cbl D2, and Cbl F3 deficiencies

-Methyl-Cbl specific deficiencies: Cbl D-Var1, Cbl E, and Cbl G deficiencies

-Transcobalamin II deficiency

-Adenosylhomocysteinase (AHCY) deficiency

-Glycine N-methyltransferase (GNMT) deficiency

-Methionine adenosyltransferase (MAT) I/III deficiency

Screening and monitoring patients suspected of or confirmed with an inherited disorder of methionine metabolism

Evaluating individuals with suspected deficiency of vitamin B12 or folate

Method Name

Liquid Chromatography-Tandem Mass Spectrometry (LC-MS/MS)

NY State Available

Yes

Specimen

Specimen Type

Serum

Necessary Information

Patient's age and sex are required.

Specimen Required

Container/Tube:

Preferred: Red top

Acceptable: Serum gel tube

Specimen Volume: 1 mL

Collection Instructions: Centrifuge and aliquot serum into plastic vial within 4 hours of collection.

Forms

1. Biochemical Genetics Patient Information (T602) in Special Instructions.

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

Specimen Minimum Volume

0.10 mL

Reject Due To

Gross hemolysis	OK
Gross lipemia	OK
Gross icterus	OK

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Serum	Refrigerated (preferred)	28 days	
	Frozen	309 days	
	Ambient	28 days	

Clinical and Interpretive

Clinical Information

Homocysteine is an intermediary in the sulfur-amino acid metabolism pathways, linking the methionine cycle to the folate cycle. Inborn errors of metabolism that lead to homocysteinemia or homocystinuria include cystathionine beta-synthase deficiency (homocystinuria) and various defects of methionine remethylation. Genetic defects in vitamin cofactors (vitamins B6, B12, and folate) and nutritional deficiency of vitamin B12 and folate also lead to abnormal homocysteine accumulation.

Homocysteine concentration is an indicator of acquired folate or cobalamin deficiency and is a contributing factor in the pathogenesis of neural tube defects. Homocysteine was also thought to be an independent predictor of cardiovascular disease (atherosclerosis, heart disease, thromboembolism), as early observational studies prior to the year 2000 linked homocysteine to cardiovascular risk and morbidity and mortality. However, following U.S. Food and Drug Administration mandated folic acid supplementation in 1998, homocysteine concentrations decreased by approximately 10% without a similar change in cardiovascular or ischemic events. Currently, the use of homocysteine for assessment of cardiovascular risk is uncertain and controversial. Based on several meta-analyses, at present, homocysteine may be regarded as a weak risk factor for coronary heart disease, and there is a lack of direct causal relationship between hyperhomocysteinemia and cardiovascular disease. It is most likely an indicator of poor lifestyle and diet.

This test should be used in conjunction with plasma amino acids, quantitative acylcarnitines, methylmalonic acid, and

urine organic acids to aid in the biochemical screening for primary and secondary disorders of methionine metabolism.

Reference Values

Age	Total Homocysteine (nmol/mL)	
	Female	Male
0-11 months	3.1-8.3	3.2-9.7
12-23 months	3.2-8.3	3.3-9.6
24-35 months	3.2-8.2	3.3-9.6
3 years	3.2-8.2	3.3-9.6
4 years	3.3-8.2	3.4-9.5
5 years	3.4-8.1	3.5-9.4
6 years	3.5-8.1	3.6-9.4
7 years	3.5-8.1	3.7-9.4
8 years	3.6-8.2	3.8-9.3
9 years	3.7-8.2	3.9-9.4
10 years	3.8-8.3	4.1-9.4
11 years	3.9-8.4	4.3-9.4
12 years	3.9-8.6	4.4-9.5
13 years	4.0-8.7	4.6-9.6
14 years	4.1-8.8	4.8-9.7
15 years	4.2-8.9	5.0-9.8
16 years	4.2-9.1	5.2-9.9
17 years	4.3-9.2	5.4-10.0
18 years	4.3-9.3	5.6-10.1
19 years	4.4-9.5	5.7-10.3
20 years	4.4-9.6	5.9-10.5
21 years	4.4-9.8	6.0-10.6
22 years	4.4-9.9	6.1-10.8
23 years	4.4-10.1	6.2-11.0
24 years	4.4-10.3	6.2-11.1
25 years	4.4-10.4	6.3-11.3
26 years	4.4-10.6	6.3-11.4
27 years	4.3-10.8	6.4-11.6
28 years	4.3-11.0	6.4-11.7
29 years	4.3-11.2	6.4-11.8
30 years	4.3-11.4	6.4-11.9
31 years	4.4-11.6	6.4-12.1
32 years	4.4-11.8	6.4-12.2
33 years	4.4-11.9	6.4-12.3

34 years	4.5-12.1	6.4-12.4
35 years	4.5-12.2	6.4-12.6
36 years	4.6-12.4	6.4-12.8
37 years	4.6-12.5	6.4-12.9
38 years	4.7-12.7	6.4-13.1
39 years	4.7-12.8	6.4-13.2
40 years	4.8-13.0	6.5-13.4
41 years	4.8-13.2	6.5-13.5
42 years	4.8-13.4	6.5-13.7
43 years	4.9-13.5	6.6-13.9
44 years	4.9-13.7	6.6-14.0
45 years	4.9-13.9	6.6-14.2
46 years	4.9-14.0	6.7-14.4
47 years	4.9-14.2	6.7-14.5
48 years	5.0-14.3	6.8-14.7
49 years	5.0-14.4	6.8-14.9
50 years	5.0-14.5	6.8-15.0
51 years	5.1-14.6	6.8-15.2
52 years	5.1-14.7	6.9-15.4
53 years	5.1-14.8	6.9-15.5
54 years	5.2-14.9	6.9-15.6
55 years	5.2-15.0	6.9-15.7
56 years	5.3-15.0	6.9-15.8
57 years	5.3-15.1	6.9-15.9
58 years	5.3-15.2	6.9-16.0
59 years	5.4-15.2	6.9-16.0
60 years	5.4-15.3	6.9-16.1
61 years	5.4-15.4	7.0-16.2
62 years	5.5-15.4	7.0-16.2
63 years	5.5-15.5	7.0-16.3
64 years	5.6-15.5	7.1-16.3
65 years	5.6-15.6	7.1-16.3
66 years	5.7-15.6	7.1-16.3
67 years	5.7-15.7	7.2-16.3
68 years	5.8-15.7	7.2-16.3
69 years	5.9-15.7	7.2-16.3
70 years	6.0-15.8	7.3-16.3
71 years	6.1-15.8	7.3-16.3
72 years	6.2-15.8	7.3-16.3

73 years	6.3-15.9	7.3-16.3
74 years	6.4-15.9	7.3-16.3
75 years	6.5-15.9	7.3-16.3
76 years	6.6-15.9	7.3-16.3
77 years	6.7-16.0	7.4-16.3
78 years	6.8-16.0	7.4-16.3
79 years	6.9-16.0	7.5-16.3
80 years	7.0-16.0	7.5-16.3
81 years	7.1-16.0	7.7-16.2
82 years	7.2-16.0	7.8-16.2
83 years	7.2-16.0	7.9-16.2
84 years	7.3-16.0	8.0-16.2
85 years	7.3-16.0	8.2-16.2
>85 years	7.4-16.0	8.3-16.2

Interpretation

Elevated homocysteine concentrations are considered informative in patients evaluated for suspected nutritional deficiencies (vitamin B12, folate) and inborn errors of metabolism. Measurement of methylmalonic acid (MMA) distinguishes between vitamin B12 (cobalamin) and folate deficiencies, as MMA is only elevated in vitamin B12 deficiency. Treatment response can be evaluated by monitoring serum homocysteine concentrations over time.

Cautions

Other factors that may influence and increase serum homocysteine include:

-Age

-Smoking

-Poor diet/cofactor deficiencies

-Chronic kidney disease/renal disease

-Hypothyroidism

Medications that may increase homocysteine concentrations include:

Medication	Effect
Methotrexate	5-Methyltetrahydrofolate depletion
Azuridine	Vitamin B6 antagonist
Nitrous oxide	Inactivation of methionine synthase
Phenytoin	Interference with folate metabolism
Carbamazepine	Interference with folate metabolism

Oral contraceptives	Estrogen-induced vitamin B6 deficiency

Clinical Reference

1. Mudd SH, Levy HL, Kraus JP: Disorders of transsulfuration. In: Valle D, Antonarakis S, Ballabio A, Beaudet AL, Mitchell GA, eds. The Online Metabolic and Molecular Bases of Inherited Disease. McGraw-Hill, 2019. Accessed October 16, 2019. Available at https://ommbid.mhmedical.com/content.aspx?sectionid=225084718&bookid=2709

2. Chrysant SG, Chrysant GS: The current status of homocysteine as a risk factor for cardiovascular disease: a mini review. Expert Rev Cardiovasc Ther. 2018;16(8):559â€“565. doi: 10.1080/14779072.2018.1497974

3. Refsum H, Smith AD, Ueland PM, et al: Facts and recommendations about total homocysteine determinations: an expert opinion. Clin Chem. 2004 Jan;50:3-32

4. Turgeon CT, Magera MJ, Cuthbert CD, et al: Determination of total homocysteine, methylmalonic acid, and 2-methylcitric acid in dried blood spots by tandem mass spectrometry. Clin Chem. 2010 Nov;56:1686-1695

5. Sacharow SJ, Picker JD, Levy HL: Homocystinuria caused by cystathionine beta-synthase deficiency. In: Adam MP, Ardinger HH, Pagon RA, et al, eds. GeneReviews [Internet] University of Washington, Seattle. 2004. Updated May 18, 2017. Accessed September 11, 2020. Available at www.ncbi.nlm.nih.gov/books/NBK1524/

Performance

Method Description

Total homocysteine is measured by stabile isotope dilution microflow liquid chromatography tandem mass spectrometry.(Unpublished Mayo method)

PDF Report

No

Day(s) Performed

Monday through Friday

Report Available

3 to 5 days

Specimen Retention Time

1 week

Performing Laboratory Location

Rochester

Fees and 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 Regional Manager. For assistance, contact Customer Service.

Test Definition: HCYSS

Homocysteine, Total, S

Test Classification

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

CPT Code Information

83090

LOINC® Information

Test ID	Test Order Name	Order LOINC Value
HCYSS	Homocysteine, Total, S	13965-9

Result ID	Test Result Name	Result LOINC Value
35836	Homocysteine, Total, S	13965-9