Overview

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

- Cystathionine beta-synthase deficiency (homocystinuria)
- Methylene tetrahydrofolate 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

Method Name
Liquid Chromatography-Tandem Mass Spectrometry (LC-MS/MS) Stable Isotope Dilution Analysis

NY State Available
Yes

Specimen

Specimen Type
Plasma EDTA

Specimen Required

**Patient Preparation:** Fasting (12 hours preferred but not required)

Container/Tube:

- **Preferred:** Lavender top (EDTA)
- **Acceptable:** Plasma Preparation Tube (PPT), citrate, sodium fluoride, heparin

**Specimen Volume:** 0.4 mL

Collection Instructions:
1. Immediately place specimen on wet ice.

2. Spin down and separate plasma from cells within 4 hours of draw. A refrigerated centrifuge is not required if 4-hour time restraint is met.

3. Alternatively, if blood is not immediately placed on ice, plasma must be removed from cells within 1 hour of draw. A refrigerated centrifuge is not required if 1-hour time restraint is met.

**Specimen Minimum Volume**

0.15 mL

**Reject Due To**

<table>
<thead>
<tr>
<th>Condition</th>
<th>Acceptance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemolysis</td>
<td>Mild OK; Gross OK</td>
</tr>
<tr>
<td>Lipemia</td>
<td>Mild OK; Gross OK</td>
</tr>
<tr>
<td>Icterus</td>
<td>Mild OK; Gross OK</td>
</tr>
<tr>
<td>Other</td>
<td>NA</td>
</tr>
</tbody>
</table>

**Specimen Stability Information**

<table>
<thead>
<tr>
<th>Specimen Type</th>
<th>Temperature</th>
<th>Time</th>
</tr>
</thead>
<tbody>
<tr>
<td>Plasma EDTA</td>
<td>Refrigerated (preferred)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Frozen</td>
<td></td>
</tr>
</tbody>
</table>

**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 (vitamin B6, B12, and folate) and nutritional deficiency of 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 also was thought to be an independent predictor of cardiovascular disease (atherosclerosis, heart disease, thromboembolism), as early observational studies prior to 2000 linked homocysteine to cardiovascular risk and morbidity and mortality. However, following FDA-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 and urine organic acids to aid in the biochemical screening for primary and secondary disorders of methionine metabolism.

**Reference Values**
Test Definition: HCYSP
Homocysteine, Total, P

Interpretation
Homocysteine concentrations >13 mcmol/L are considered abnormal in patients evaluated for suspected nutritional deficiencies (B12, folate) and inborn errors of metabolism. Measurement of methylmalonic acid (MMA) distinguishes between B12 (cobalamin) and folate deficiencies, as MMA is only elevated in B12 deficiency. Response to dietary treatment can be evaluated by monitoring plasma homocysteine concentrations over time.

Homocysteine concentrations < or =10 mcmol/L are desirable when utilized for cardiovascular risk.

Cautions
A fasting specimen is recommended; however, nonfasting homocysteine concentrations produce slightly higher, but likely clinically insignificant changes.

Other factors that may influence and increase plasma homocysteine include:
- Age
- Smoking
- Poor diet/cofactor deficiencies
- Chronic kidney disease/renal disease
- Hypothyroidism

Medications that may increase homocysteine concentrations include:

<table>
<thead>
<tr>
<th>Medication</th>
<th>Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Methotrexate</td>
<td>5-Methyltetrahydrofolate depletion</td>
</tr>
<tr>
<td>Azuridine</td>
<td>Vitamin B6 antagonist</td>
</tr>
<tr>
<td>Nitrous Oxide</td>
<td>Inactivation of methionine synthase</td>
</tr>
<tr>
<td>Phenytoin</td>
<td>Interference with folate metabolism</td>
</tr>
<tr>
<td>Carbamazepine</td>
<td>Interference with folate metabolism</td>
</tr>
<tr>
<td>Oral Contraceptives</td>
<td>Estrogen-induced vitamin B6 deficiency</td>
</tr>
</tbody>
</table>

Clinical Reference
Homocysteine, Total, P


Performance

Method Description
One hundred microliters of plasma are spiked with d(8)-homocystine (2 nmoles) added as internal standard. After specimen reduction and deproteinization, the analysis by tandem mass spectrometry is performed in the multiple reaction monitoring mode. (Magera MJ, Lacey JM, Casetta B, Rinaldo P: A method for the determination of total homocysteine in plasma and urine by stable isotope dilution and electrospray tandem mass spectrometry. Clin Chem 1999;45:1517-1522)

PDF Report
No

Day(s) and Time(s) Test Performed
Monday through Saturday; 8 a.m.

Analytic Time
2 days (not reported Sundays)

Maximum Laboratory Time
4 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 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 U.S. Food and Drug Administration.

CPT Code Information
83090
# Test Definition: HCYSP

**Homocysteine, Total, P**

## LOINC® Information

<table>
<thead>
<tr>
<th>Test ID</th>
<th>Test Order Name</th>
<th>Order LOINC Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>HCYSP</td>
<td>Homocysteine, Total, P</td>
<td>13965-9</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Result ID</th>
<th>Test Result Name</th>
<th>Result LOINC Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>80379</td>
<td>Homocysteine, Total, P</td>
<td>13965-9</td>
</tr>
</tbody>
</table>