Overview

Useful For
Investigation of suspected folate deficiency

Testing Algorithm
See Vitamin B12 Deficiency Evaluation in Special Instructions.

Special Instructions
- Vitamin B12 Deficiency Evaluation

Method Name
Competitive-Binding Receptor Assay

NY State Available
Yes

Specimen

Specimen Type
Serum

Specimen Required

Container/Tube:
- Preferred: Serum gel
- Acceptable: Red top

Specimen Volume: 0.6 mL

Collection Instructions:
1. Fasting (8 hours)
2. Serum gel tubes should be centrifuged within 2 hours of collection.
3. Red-top tubes should be centrifuged and aliquoted within 2 hours of collection.

Additional Information: Do not order on patients who have recently received methotrexate or other folic acid antagonists.

Forms
If not ordering electronically, complete, print, and send a Benign Hematology Test Request Form (T755) with the specimen.

Specimen Minimum Volume
0.5 mL
Reject Due To

<table>
<thead>
<tr>
<th>Condition</th>
<th>Action</th>
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</thead>
<tbody>
<tr>
<td>Gross hemolysis</td>
<td>Reject</td>
</tr>
<tr>
<td>Gross lipemia</td>
<td>OK</td>
</tr>
</tbody>
</table>

Specimen Stability Information

<table>
<thead>
<tr>
<th>Specimen Type</th>
<th>Temperature</th>
<th>Time</th>
<th>Special Container</th>
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</thead>
<tbody>
<tr>
<td>Serum</td>
<td>Refrigerated (preferred)</td>
<td>7 days</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Frozen</td>
<td>90 days</td>
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Clinical and Interpretive

Clinical Information

The term folate refers to all derivatives of folic acid. For practical purposes, serum folate is almost entirely in the form of $N\-(5)$-methyl tetrahydrofolate.(1)

Approximately 20% of the folate absorbed daily is derived from dietary sources; the remainder is synthesized by intestinal microorganisms. Serum folate levels typically fall within a few days after dietary folate intake is reduced and may be low in the presence of normal tissue stores. RBC folate levels are less subject to short-term dietary changes.

Significant folate deficiency is characteristically associated with macrocytosis and megaloblastic anemia. Lower than normal serum folate also has been reported in patients with neuropsychiatric disorders, in pregnant women whose fetuses have neural tube defects, and in women who have recently had spontaneous abortions.(2) Folate deficiency is most commonly due to insufficient dietary intake and is most frequently encountered in pregnant women or in alcoholics.

Other causes of low serum folate concentration include:

- Excessive utilization (eg, liver disease, hemolytic disorders, and malignancies)
- Rare inborn errors of metabolism (eg, dihydrofolate reductase deficiency, formiminotransferase deficiency, 5,10-methylenetetrahydrofolate reductase deficiency, and tetrahydrofolate methyltransferase deficiency)

Reference Values

> or $\geq 4.0$ mcg/L

<4.0 mcg/L suggests folate deficiency

Interpretation

Serum folate is a relatively nonspecific test.(3) Low serum folate levels may be seen in the absence of deficiency and normal levels may be seen in patients with macrocytic anemia, dementia, neuropsychiatric disorders, and pregnancy disorders.

Results <4 mcg/L are suggestive of folate deficiency. The cutoff is based on consensus and was derived from the US NHANES III data.(4)
Evaluation of macrocytic anemias commonly requires measurement of the serum concentration of both vitamin B12 and folate; ideally they should be measured at the same point in time.

Serum folate measurement is preferred over RBC folate measurement due to considerable analytic variability (coefficient of variation: CV) of assays. Both results give the same interpretation (internal Mayo study) therefore RBC folate quantitation is not recommended. Additional serum testing with homocysteine and methylmalonic acid (MMA) determinations may help distinguish between vitamin B12 and folate deficiency states. In folate deficiency, homocysteine levels are elevated and MMA levels are normal. In vitamin B12 deficiency, the analytic variability (CV) of both serum and RBC folate assays is considerable. Homocysteine and MMA levels are alternate determinates of folate deficiency.

See Vitamin B12 Deficiency Evaluation in Special Instructions.

Cautions

Patients with combined deficiency of folate and iron may not demonstrate the erythrocyte macrocytosis that is typical of folate deficiency anemia. In these patients, however, the red cell distribution width (RDW) will typically be elevated.

Nonfasting specimens yield falsely elevated results.

Recent folic acid administration or dietary folate intake could result in normal or elevated values and possibly mask an underlying folate deficiency.

Folates other than N-(5)-methyltetrahydrofolate and folic acid antagonists (such as methotrexate) may, under some circumstances, be present in serum and will also be measured by this method.

Some patients who have been exposed to animal antigens, either in the environment or as part of treatment or imaging procedures, may have circulating antianimal antibodies present. These antibodies may interfere with the assay reagents to produce unreliable results.

Clinical Reference


Performance

Method Description

The instrument used is a Beckman Coulter DXI 800. The Access Folate assay is a competitive-binding receptor assay. A serum specimen is treated to release folate from endogenous binding proteins. After neutralization of the reaction mixture, folate-binding protein, mouse antifolate-binding protein, folic acid-alkaline phosphatase conjugate,
and goat antimouse capture antibody coupled to paramagnetic particles are added to the reaction vessel. Folate in the sample competes with the folic acid-alkaline phosphatase conjugate for binding sites on a limited amount of folate-binding protein. Resulting complexes bind to the solid phase via mouse antifolate binding protein. After incubation in a reaction vessel, materials bound to the solid phase are held in a magnetic field, while unbound materials are washed away. The chemiluminescent substrate Lumi-Phos 530 is added to the vessel and light generated by the reaction is measured with a luminometer. The light production is inversely proportional to the concentration of folate in the sample. The amount of analyte in the sample is determined from a stored, multipoint calibration curve. The assay is standardized to the World Health Organization (WHO) International Standard 03/178. (Beckman Coulter Assay Manual 2011, Beckman Coulter Inc., Fullerton, CA)

**PDF Report**

No

**Day(s) and Time(s) Test Performed**

Monday through Friday; 5 a.m.-12 a.m.

Saturday; 6 a.m.-6 p.m.

**Analytic Time**

Same day/1 day

**Maximum Laboratory Time**

3 days

**Specimen Retention Time**

14 days

**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 has been cleared, approved or is exempt by the U.S. Food and Drug Administration and is used per manufacturer's instructions. Performance characteristics were verified by Mayo Clinic in a manner consistent with CLIA requirements.

**CPT Code Information**

82746

**LOINC® Information**

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<th>Test Order Name</th>
<th>Order LOINC Value</th>
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<td>Folate, S</td>
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