Test Definition: FOL

Folate, S

Overview

Useful For
Investigation of suspected folate deficiency

Testing Algorithm
For more information, see Vitamin B12 Deficiency Evaluation.

Special Instructions
- Vitamin B12 Deficiency Evaluation

Method Name
Competitive-Binding Receptor Assay

NY State Available
Yes

Specimen

Specimen Type
Serum

Specimen Required
Patient preparation:

1. Patient should be fasting for 8 hours.

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

Container/Tube:

Preferred: Serum gel

Acceptable: Red top

Specimen Volume: 0.6 mL

Collection Instructions:

1. Serum gel tubes should be centrifuged within 2 hours of collection.

2. Red-top tubes should be centrifuged and the serum aliquoted within 2 hours of collection.

Forms

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

Reject Due To

Gross hemolysis	Reject
Gross lipemia	OK

Specimen Minimum Volume

0.5 mL

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Serum	Refrigerated (preferred)	7 days	
	Frozen	90 days	

Clinical & 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 =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 below 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) 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 of both serum and RBC folate assays is considerable. Homocysteine and MMA levels are alternate determinates of folate deficiency.

For more information, see Vitamin B12 Deficiency Evaluation.

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 anti-animal antibodies present. These antibodies may interfere with the assay reagents to produce unreliable results.

Clinical Reference

1. Fairbanks VF, Klee GG: Biochemical aspects of hematology. In: Burtis CA, Ashwood ER, eds: Tietz Textbook of Clinical Chemistry. Saunders Company; 1999:1690-1698

2. George L, Mills JL, Johansson AL, et al: Plasma folate levels and risk of spontaneous abortion. JAMA 2002 October 16;288:1867-1873

3. Klee GG: Cobalamin and folate evaluation: measurement of methylmalonic acid and homocysteine vs vitamin B12 and folate. Clin Chem. 2000 August;46(8 Pt 2):1277-1283

4. Benoist BD: Conclusions of a WHO Technical Consultation on folate and vitamin B12 deficiencies. Food and Nutrition Bulletin 2008 (volume 29, number 2) S238-S244

5. Roberts NB, Taylor A, Sodi R: Vitamins and trace elements. In: Rifai N, Horvath AR, Wittwer CT, eds. Tietz Textbook of Clinical Chemistry and Molecular Diagnostics. 6th ed. Elsevier; 2018:chap 37

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

Specimen Retention Time
14 days

Performing Laboratory Location
Rochester

Fees & Codes

Test Classification
This test has been cleared, approved, or is exempt by the US 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

Test ID	Test Order Name	Order LOINC Value
FOL	Folate, S	2284-8

Result ID	Reporting Name	LOINC®
FOL	Folate, S	2284-8