Test Definition: MMAU

Methylmalonic Acid, Quantitative, Urine

Overview

Useful For

Evaluating children with signs and symptoms of methylmalonic acidemia using urine specimens

Evaluating individuals with signs and symptoms associated with a variety of causes of vitamin B12 (cobalamin) deficiency

Method Name

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

NY State Available

Yes

Specimen

Specimen Type

Urine

Specimen Required

Patient Preparation:

Fasting: 8 hours, required

Supplies: Urine Tubes, 10 mL (T068)

Container/Tube: Plastic, 10-mL urine tube

Specimen Volume: 4 mL

Collection Instructions:

1. After fasting at least 8 hours overnight, patient should void first-morning urine as normal. **Do not collect**.
2. Patient should continue to fast and then collect the next (second morning) urine voided.

Forms

If not ordering electronically, complete, print, and send 1 of the following forms with the specimen:

-Biochemical Genetics Test Request (T798)

-Benign Hematology Test Request (T755)

Specimen Minimum Volume

1.2 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 (preferred)	28 days	
	Ambient	21 days	
	Refrigerated	28 days	

Clinical & Interpretive

Clinical Information

Elevated levels of methylmalonic acid (MMA) result from inherited defects of enzymes involved in MMA metabolism or inherited or acquired deficiencies of vitamin B12 (cobalamin) or its downstream metabolites. Acquired deficiencies of vitamin B12 are much more common and can be due to intestinal malabsorption, impaired digestion, or poor diet. Older adult patients with cobalamin deficiency may present with peripheral neuropathy, ataxia, loss of position and vibration senses, memory impairment, depression, and dementia in the absence of anemia. Other conditions such as kidney insufficiency, hypovolemia, and bacterial overgrowth of the small intestine also contribute to the possible causes of mild methylmalonic acidemia and aciduria.

Methylmalonic acid is also a specific diagnostic marker for the group of disorders collectively called methylmalonic acidemia, which include at least 7 different complementation groups. Two of them (mut0 and mut-) reflect deficiencies of the apoenzyme portion of the enzyme methylmalonyl-CoA mutase. Two other disorders (CblA and CblB) are associated with abnormalities of the adenosylcobalamin synthesis pathway. CblC, CblD, and CblF deficiencies lead to impaired synthesis of both adenosyl- and methylcobalamin.

Since the first reports of this disorder in 1967, thousands of cases have been diagnosed worldwide. Newborn screening identifies approximately 1 in 30,000 live births with a methylmalonic acidemia. The most frequent clinical manifestations are neonatal or infantile metabolic ketoacidosis, failure to thrive, and developmental delay. Excessive protein intake may cause life-threatening episodes of metabolic decompensation and remains a lifelong risk unless treatment is closely monitored, which includes serum and urine MMA levels.

Several studies have suggested that the determination of serum or urinary methylmalonic acid could be a more reliable marker of vitamin B12 deficiency than direct vitamin B12 determination.

Reference Values

<3.60 mmol/mol creatinine

Interpretation

In pediatric patients, markedly elevated methylmalonic acid values indicate a probable diagnosis of methylmalonic acidemia. Additional confirmatory testing must be performed.

In adults, moderately elevated values indicate a likely vitamin B12 (cobalamin) deficiency.

Cautions

Diet, nutritional status, and age should be considered in the evaluation of serum or urine methylmalonic acid level.

Clinical Reference

1. Fenton WA, Gravel RA, Rosenblatt DS. Disorders of propionate and methylmalonate metabolism. 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 December 16, 2025. Available at https://ommbid.mhmedical.com/content.aspx?sectionid=225086103&bookid=2709

2. Klee GG. Cobalamin and folate evaluation: Measurement of methylmalonic acid and homocysteine vs vitamin B(12) and folate. Clin Chem. 2000;46(8 Pt 2):1277-1283

3. Watkins D, Rosenblatt DS. Inherited disorders of folate and cobalamin transport and metabolism. In: Valle D, Antonarakis S, Ballabio A, Beaudet AL, Mitchell GA, eds. The Online Metabolic and Molecular Basis of Inherited Disease. McGraw-Hill; 2019. Accessed December 16, 2025. Available at https://ommbid.mhmedical.com/content.aspx?sectionid=225548307&bookid=2709

4. Vashi P, Edwin P, Popiel B, Lammersfeld C, Gupta D. Methylmalonic acid and homocysteine as indicators of vitamin B-12 deficiency in cancer. PLoS One. 2016;11(1):e0147843

Performance

Method Description

Methylmalonic acid (MMA) is determined by liquid chromatography tandem mass spectrometry (LC-MS/MS) stable isotope dilution analysis. The specimen is mixed with an internal standard (methyl-d3-malonic acid). MMA and d3-MMA are isolated by solid phase extraction. LC-MS/MS is performed using mobile phases and a short column to separate MMA and d3-MMA from the bulk of the specimen matrix. The MS/MS is operated in the multiple reaction monitoring (MRM) negative mode to follow the precursor to product species transitions. Separation of MMA/d3-MMA from the more physiologically abundant succinic acid is accomplished by the careful selection of MRM transitions and optimization of the LC separation. The ratios of the extracted peak areas of MMA to d3-MMA determined by LC-MS/MS are used to calculate the concentration of MMA present in the sample.(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

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

83921

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
MMAU	Methylmalonic Acid, QN, U	25116-5

Result ID	Test Result Name	Result LOINC® Value
80290	Methylmalonic Acid, QN, U	25116-5