

Testing Notification

December 2013

Important Information for Providers

MTHFR (5919/MTR) polymorphism testing no longer orderable

Due to lack of clinical utility, effective immediately, MTHFR (5919/MTR) polymorphism testing will no longer be orderable. Orders received will be cancelled.

The preferred test for hyperhomocysteinemia is a fasting plasma homocysteine level 4775/HOM (LAB4775).

MTHFR variants are not risk factors for venous thromboembolism or recurrent pregnancy loss

Recent studies and meta-analyses have disproven an association between MTHFR variants and venous thromboembolism or recurrent pregnancy loss. Also, MTHFR variants do not add to the risk of recurrent thromboembolism in patients with Factor V Leiden or other thrombophilic conditions. The lack of evidence to support MTHFR variant testing is detailed in a 2013 practice guideline from the American College of Medical Genetics and Genomics (ACMG)¹.

ACMG RECOMMENDATIONS:

- MTHFR polymorphism genotyping should not be ordered as part of the clinical evaluation for thrombophilia or recurrent pregnancy loss
- MTHFR polymorphism genotyping should not be ordered for at-risk family members
- MTHFR status does not change the recommendation that women of childbearing age should take the standard dose of folic acid supplementation to reduce the risk of neural tube defects as per the general population guidelines

MTHFR testing lacks clinical utility for hyperhomocysteinemia

MTHFR variants have mildly reduced enzyme activity that predisposes to hyperhomocysteinemia, but only in the presence of low serum folate levels. Following FDA-mandated folic acid supplementation in 1998, folate deficiency has

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become rare and the association of MTHFR variants with hyperhomocysteinemia has essentially disappeared.

Multiple factors can cause elevated homocysteine and risks from hyperhomocysteinemia are independent of MTHFR status. Vitamins B6 (pyridoxine) and B12 also regulate homocysteine and physiologic and environmental factors play a role. The presence of an MTHFR variant does not alter risks or treatment. Therefore, the most informative test for hyperhomocysteinemia is a fasting plasma homocysteine level [4775/HOM \(LAB4775\)](#).

MTHFR variant testing for rare genetic or pharmacogenomic indications would require AHL medical director approval by calling 612-863-4678.

References:

1. Hickey SE, Curry CJ, Toriello HV, ACMG Practice Guideline: lack of evidence for MTHFR polymorphism testing. Genet Med. 2013 Feb;15(2):153-6. doi: 10.1038/gim.2012.165. Epub 2013 Jan 3
2. Bezemer ID, Doggen CJ, Vos HL, Rosendaal FR., No association between the common MTHFR 677C->T polymorphism and venous thrombosis: results from the MEGA study. Arch Intern Med. 2007 Mar 12;167(5):497-501
3. Mayo Medical Laboratories Website: <http://www.mayomedicallaboratories.com/test-catalog/Clinical+and+Interpretive/80379>

For questions, comments, or suggestions about this newsletter or other laboratory issues, please contact Lauren Anthony, MD, Medical Director of Allina Health Laboratory, (612) 863-0409 or Lauren.Anthony@allina.com