MAYO CLINIC LABORATORIES

# Test Definition: MEVI

Methemoglobinemia Interpretation

## Overview

### Useful For

Interpretation of the methemoglobinemia evaluation results
Diagnosis of methemoglobinemia and sulfhemoglobinemia and possible hereditary (congenital) causes
Differentiation of methemoglobinemia and sulfhemoglobinemia from other causes of cyanosis (eg, congenital heart disease)

### Method Name

Only orderable as part of a profile. For more information see MEV1 / Methemoglobinemia Evaluation.
Medical Interpretation

### NY State Available

Yes

## Specimen

### Specimen Type

Whole Blood EDTA

### Specimen Stability Information

| Specimen Type | Temperature | Time | Special Container |
|---|---|---|---|
| Whole Blood EDTA | Refrigerated (preferred) | | |

## Clinical & Interpretive

### Clinical Information

Methemoglobin:
Methemoglobin forms when the hemoglobin molecule iron is in the ferric (Fe[3+]) form instead of the functional ferrous (Fe[2+]) form. Methemoglobinemia can be hereditary or acquired and is present by definition when methemoglobin levels are greater than the normal range. Acquired methemoglobinemia results after toxic exposure to nitrates and nitrites/nitrates (fertilizer, nitric oxide), topical anesthetics (“caines"), dapsone, naphthalene (moth balls/toilet deodorant cakes), and industrial use of aromatic compounds (aniline dyes).
Congenital methemoglobinemias are rare. They are due either to:
-A deficiency of cytochrome b5 reductase (methemoglobin reductase) in erythrocytes, an autosomal recessive disorder resulting from genetic variants in either *CYB5R3* or *CYB5A* genes.(1,2) Type IV is thought to be extraordinarily rare. Type III is no longer a category.
-One of several intrinsic structural disorders of hemoglobin, called M-hemoglobins (M-Hb), all of which are inherited in an autosomal dominant manner.(3,4) Classically, M-Hb result from histidine-to-tyrosine substitutions at the proximal or distal histidine important in coordinating the oxygen molecule. These include alpha-, beta- and gamma-chain variants. Rarely, other substitutions outside the proximal and distal histidine location can cause hemoglobin variants that increase

methemoglobin or sulfhemoglobin levels. Most M-Hb variants are readily identified by high-performance liquid chromatography (HPLC) or mass spectrometry methods with characteristic electrophoresis patterns; however, some require more specialized techniques. Most are associated with increased methemoglobin, with or without an increase in sulfhemoglobin. Alpha chain M-Hb variants can be associated with increased sulfhemoglobin without an increase in methemoglobin.

Sulfhemoglobin:

Sulfhemoglobin cannot combine with oxygen. When acquired, sulfhemoglobinemia can be associated with cyanosis and often accompanies methemoglobinemia. Sulfhemoglobinemia has been associated with exposure to sumatriptan, sulfonamides, metoclopramide, paint or varnish vapors, dimethyl sulfoxide (DMSO), acetanilide, phenacetin, trinitroluene, zinc ethylene bisdithiocarbamate (a fungicide), and flutamide. It is important to note that some hemoglobin variants are known to interfere with this test (especially M-Hb), and sulfhemoglobin absorbance can be increased due to the hemoglobin variant. Hemoglobin evaluation that includes the HPLC method is recommended to exclude this possibility.

In contrast to methemoglobinemia, sulfhemoglobinemia persists until the erythrocytes containing it are destroyed. Therefore, blood level of sulfhemoglobin declines gradually over a period of weeks.

## Reference Values

Only orderable as part of a profile. For more information see MEV1 / Methemoglobinemia Evaluation.

Definitive results and an interpretive report will be provided.

## Interpretation

This is a consultative evaluation in which the history and previous laboratory values are reviewed by a hematologist who is an expert on these disorders. Appropriate tests are performed and an interpretive report is issued.

## Cautions

Sulfhemoglobin is exceedingly stable and does not change in stored or shipped specimens.

Methemoglobin is unstable and can degrade at a rate of about 40% per 24 hours.

A normal methemoglobin value obtained with stored or shipped specimens does not exclude prior methemoglobinemia of minimal degree. However, significant methemoglobinemia will still be demonstrable.

## Clinical Reference

1. OMIM: 250800 Methemoglobinemia due to deficiency of methemoglobin reductase. Updated May 20, 2019. Accessed October 19, 2020. Available at www.omim.org/entry/250800?search=250800&highlight=250800

2. OMIM: 250790 Methemoglobinemia and ambiguous genitalia. Updated May 18, 2018. Accessed October 19, 2020. Available at www.omim.org/entry/250790?search=250790&highlight=250790

3. OMIM: 141800 Hemoglobin alpha locus 1; HBA1. Updated November 1, 2019. Accessed October 19, 2020. Available at www.omim.org/entry/141800?search=141800&highlight=141800

4. OMIM: 141900 Hemoglobin beta locus; HBB. Updated November 14, 2019. Accessed October 19, 2020. Available at www.omim.org/entry/141900?search=141900&highlight=141900

5. Haymond S, Cariappa R, Eby CS, Scott MG: Laboratory assessment of oxygenation in methemoglobinemia. Clin Chem. 2005;51(2):434-444

6. Noor M, Beutler E: Acquired sulfhemoglobinemia. An underreported diagnosis? West J Med. 1998;169(6):386-389

7. Thom CS, Dickson CF, Gell DA, Weiss MJ: Hemoglobin variants: biochemical properties and clinical correlates. Cold Spring Harb Perspect Med. 2013;3(3):a011858

8. Percy MJ, McFerran NV, Lappin TR: Disorders of oxidized haemoglobin. Blood Rev. 2005;19(2):61-68

9. Agarwal AM, Prchal JT: Methemoglobinemia and other dyshemoglobinemias. In: Kaushansky K, Lichtman MA, Prchal JT, et al. eds. Williams Hematology. 9th ed. McGraw-Hill Book Company; 2016:789-800

# Test Definition: MEVI

Methemoglobinemia Interpretation

## Performance

### Method Description
A hematopathologist who is an expert in these disorders evaluates the case and an interpretive report is issued.

### PDF Report
No

### Specimen Retention Time

### Performing Laboratory Location
Rochester

## Fees & Codes

### Test Classification
Not Applicable

### CPT Code Information
83020-26