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	72 hours	

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 January 22, 2024. Available at www.omim.org/entry/250800?search=250800&highlight=250800
2. OMIM: 250790 Methemoglobinemia and ambiguous genitalia. Updated December 9, 2022. Accessed January 22,

2024. Available at www.omim.org/entry/250790?search=250790&highlight=250790
3. OMIM: 141800 Hemoglobin alpha locus 1; HBA1. Updated September 15, 2023. Accessed January 22, 2024. Available at www.omim.org/entry/141800?search=141800&highlight=141800
4. OMIM: 141900 Hemoglobin beta locus; HBB. Updated September 15, 2023. Accessed January 22, 2024. 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

Performance

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

PDF Report
No

Day(s) Performed
Monday through Friday

Report Available
3 to 25 days

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
Not Applicable

CPT Code Information

83020-26

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
MEVI	Methemoglobinemia Interpretation	59466-3

Result ID	Test Result Name	Result LOINC® Value
608086	Methemoglobinemia Interpretation	59465-5
608108	Reviewed By	18771-6