Test Definition: METR1

Cytochrome b5 Reductase Enzyme Activity, Blood

Overview

Useful For

Evaluation of patients with cyanosis

Confirming cases of suspected cytochrome b5 reductase (methemoglobin reductase) deficiency

Functional studies in families with cytochrome b5 reductase deficiency

Method Name

Kinetic Spectrophotometry (KS)

NY State Available

Yes

Specimen

Specimen Type

Whole Blood ACD-B

Specimen Required

Collection Container/Tube:
Preferred: Yellow top (ACD)
Acceptable: Lavender top (EDTA)
Specimen Volume: 6 mL
Collection Instructions: Send whole blood specimen in original tube. **Do not aliquot.**

Forms

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

Specimen Minimum Volume

1 mL

Reject Due To

Gross hemolysis	Reject
Fully clotted	Reject

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Whole Blood ACD-B	Refrigerated	18 days	

Clinical & Interpretive

Clinical Information

Cytochrome b5 reductase (CYB5R), also called methemoglobin reductase, is the enzyme within the erythrocyte that maintains hemoglobin in the reduced (non-methemoglobin) state. A deficiency of CYB5R in erythrocytes is an autosomal recessive disorder resulting from variants in the *CYB5R3* or the *CYB5A* genes.

Persons who are heterozygous for CYB5R genetic variants have no clinical or laboratory abnormalities, are not cyanotic, and have normal methemoglobin concentrations in their blood. However, they hold an increased risk for more severely symptomatic acute episodes of methemoglobinemia with exposure to inducing agents.

Persons who are homozygous for CYB5R genetic variants have normal arterial oxygen saturation but have varying quantities of methemoglobin in their blood, generally 15% to 20%, and are quite cyanotic. Paradoxically, homozygous individuals typically have normal blood counts; the condition only rarely causes polycythemia. The presence of methemoglobin shifts the hemoglobin-oxygen dissociation curve to the right, so although the transport of oxygen is diminished, the delivery of oxygen to tissues is normal. Because of the chronicity, the homozygous condition is usually compensated and, therefore, quite benign, but it may cause concern to parents of affected children, be a cosmetic embarrassment to the children, and alarm the attending physician. The cyanosis may be treated with methylene blue.

Reference Values

> or =12 months of age: 7.8-13.1 U/g Hb
Reference values have not been established for patients younger than 12 months.

Interpretation

Cytochrome b5 reductase (methemoglobin reductase) activity in neonates (0-6 weeks) is normally 60% of the normal adult value. Adult values are attained by 2 to 3 months.

Heterozygotes have results slightly lower than the reference range. Homozygotes demonstrate little to no cytochrome b5 reductase activity and increased levels of methemoglobin.

Cautions

Individuals who are glucose-6-phosphate dehydrogenase deficient are not candidates for methylene blue therapy. Administration of methylene blue to such persons will cause hemolysis or methemoglobin formation.

Clinical Reference

1. Agarwal AM, Prchal JT. Methemoglobinemia and other dyshemoglobinemias. In: Kaushansky K, Lichtman MA, Prchal JT, et al, eds. Williams Hematology. 9th ed. McGraw-Hill; 2016:789-800
2. Percy MJ, Barnes C, Crighton G, et al. Methemoglobin reductase deficiency: Novel mutation is associated with a disease phenotype of intermediate severity. J Pediatr Haematol Oncol. 2012;34:457-460

Performance

Method Description

Cytochrome b5 reductase (methemoglobin reductase) catalyzes the 1,4-dihydronicotinamide adenine dinucleotide (NADH)-linked reduction of several substrates, including ferricyanide. The activity at 37 degrees C is measured spectrophotometrically by measuring the oxidation of NADH to NAD(+) at 340 nm on an automated chemistry analyzer.(Fairbanks VF, Klee GG. Biochemical aspects of hematology. In: Burtis CA, Ashwood ER, eds. Tietz Textbook of Clinical Chemistry. 3rd ed. WB Saunders Company. 1999:1647-1648; van Solinge WW, van Wijk. Enzymes of the red blood cell. In: Rifai N, Horvath AR, Wittwer CT. eds. Tietz Textbook of Clinical Chemistry and Molecular Diagnostics. 6th ed. Elsevier; 2018:chap 30)

PDF Report

No

Day(s) Performed

Performed weekly

Report Available

1 to 6 days

Specimen Retention Time

7 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

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

82657

LOINC® Information

MAYO CLINIC LABORATORIES

Test Definition: METR1

Cytochrome b5 Reductase Enzyme Activity, Blood

Test ID	Test Order Name	Order LOINC® Value
METR1	Cytochrome b5 Reductase, B	32703-1

Result ID	Test Result Name	Result LOINC® Value
METRB	Cytochrome b5 Reductase, B	32703-1