

Oxygen Dissociation, P50

SUGGESTS THE PRESENCE OF HEMOGLOBIN VARIANTS WITH ALTERED OXYGEN AFFINITY

Disease Overview

- Mutations in the globin genes may result in hemoglobin variants with altered function, namely increased or decreased affinity for oxygen. Such mutations result in disrupted binding between the alpha and globin hemoglobin subunits or interfere with binding of 2,3-diphosphoglycerate (2,3-DPG).
- Hemoglobin variants with high oxygen affinity deliver less oxygen to peripheral tissues, leading to hypoxia and causing increased erythropoietin production, which results in benign hereditary polycythemia. Such variants are associated with increased hematocrit, increased blood hemoglobin concentration with normal leukocyte and platelet counts, and lack of splenomegaly.
- Low-oxygen-affinity variants are associated with anemia and may be accompanied by cyanosis.
- Hemoglobin variants with abnormal oxygen affinity can be identified by measuring the oxygen dissociation curve (ODC) and P50 value (partial pressure of oxygen where hemoglobin is 50 percent oxygenated).
 - High-affinity hemoglobin variants are characterized by a decreased P50 value with the sigmoidal ODC shifted to the left. Some high-affinity variants have nearly normal P50 values but a non-sigmoidal ODC.
 - Low-affinity hemoglobin variants have an increased P50 value with the sigmoidal ODC shifted to the right.
- Decreased P50 values and polycythemia may result from other disorders expressed in red blood cells including 2,3-DPG deficiency, methemoglobinemia, and carboxyhemoglobinemia from chronic smoking.
 - 2,3-DPG deficiency is a rare, autosomal recessive, congenital disorder resulting from deficiency of biphosphoglyceromutase. 2,3-DPG normally binds hemoglobin and allosterically changes its configuration to a low-oxygen-affinity state. 2,3-DPG deficiency results in increased oxygen affinity and polycythemia.
- Globin gene sequencing or hemoglobin evaluation by HPLC may be used to confirm hemoglobin variants with altered oxygen affinity.
- Identification of either high- or low-affinity hemoglobins may prevent unnecessary evaluations or potentially harmful treatments.

Epidemiology

- High-oxygen-affinity variants are rare causes of congenital polycythemia.
- Low-oxygen-affinity variants are less common than high-affinity variants.

Genetics

- Autosomal dominant inheritance, although de novo mutations have been reported.
- More than 100 high-affinity hemoglobin variants have been described; low-affinity hemoglobin variants are less common.
- Due to gene copy number, alpha globin gene mutations resulting in hemoglobins with altered oxygen affinity may have a more mild clinical effect compared with similar beta globin variants.
- Homozygotes for beta globin gene mutations resulting in high-affinity hemoglobins may be more severely affected than heterozygotes. Homozygosity for high-affinity variants caused by alpha globin mutations and homozygosity for low-affinity variants may be embryonic lethal.
- Co-inheritance of a thalassemia allele may alter clinical expression.

Indications for Ordering

- Individuals with familial polycythemia.
- Individuals with isolated polycythemia who lack a JAK2 mutation and do not exhibit clinical findings (i.e., leukocytosis, thrombocytosis, and splenomegaly) associated with polycythemia vera.
- Cyanotic individuals with or without anemia.

Interpretation

- Negative: P50 = 24–30 mmHg with sigmoidal ODC.
- Positive:
 - P50 <24 mmHg; suggests the presence of a high-oxygen-affinity hemoglobin variant.
 - P50 >30 mmHg; suggests the presence of a low-oxygen-affinity hemoglobin variant.

Limitations

- Samples must be analyzed within 48 hours of collection as P50 decreases with time.
- This assay will not distinguish between the possible causes for decreased P50, which include: 2,3-DPG deficiency, high-oxygen-affinity hemoglobin variants, methemoglobinemia, and carboxyhemoglobinemia.
- Decreased P50 values in chronic smokers (carboxyhemoglobinemia) should be interpreted with caution, as hemoglobin has higher affinity for carbonmonoxy than oxygen.
- P50 values should be correlated with age as fetal hemoglobin (HbF) may produce a decreased P50.

Methodology

Clark electrode to assess oxygen partial pressure and dual wavelength spectrophotometry to measure degree of oxygen saturation of hemoglobin. Multiple instantaneous measurements from the oxygen sensor are used to generate a full oxygen dissociation curve. P50 is determined as the partial pressure of oxygen where hemoglobin is 50 percent oxygenated.

Related Tests

- [Hemoglobin Evaluation with Reflex to Electrophoresis and/or RBC Solubility \(0050610\)](#)
- [Beta Globin \(HBB\) Sequencing \(0050578\)](#)
- [Alpha Thalassemia \(HBA1 & HBA2\) Sequencing \(2001582\)](#)

References

1. Guarnone R, et al. Performance characteristics of hemox-analyzer for assessment of the hemoglobin dissociation curve. *Haematologica* 1995;80(5):426–30.
2. Maran J and Prchal J. Polycythemia and oxygen sensing. *Pathol Biol* 2004; 52(5):280–4.
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4. Rumi E, et al. Blood p50 evaluation enhances diagnostic definition of isolated erythrocytosis. *J Intern Med* 2008;265:266–74.
5. Steinberg MH and Nagel RL. Unstable hemoglobins, hemoglobins with altered oxygen affinity, hemoglobin M, and other variants of clinical and biological interest. *Disorders of hemoglobin: genetics, pathophysiology, and clinical management*, 2nd Ed. MH Steinberg, et al, eds. 2009; New York: Cambridge University Press, 590–3.

Test Information

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For specific collection, transport, and testing information, refer to the ARUP website at www.aruplab.com.

For information on test selection, ordering, and interpretation, refer to ARUP Consult® at www.arupconsult.com.