Chromogenic Factor VIII, Activity

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Chromogenic factor VIII activity is used for the diagnosis of nonsevere hemophilia A (in conjunction with the one-stage clot-based factor VIII activity). Nonsevere hemophilia A may require both one-stage clot-based factor VIII activity and chromogenic factor VIII activity for diagnosis and severity classification due to differences in how the underlying mutations affect factor VIII activity in the tests.[1]

This assay may also be used in the measurement of factor VIII activity in the presence of interfering drugs or lupus anticoagulants that result in underestimation by clot-based methods.

For more information about the hemophilia A and the recommended laboratory testing strategy, refer to the ARUP Consult Hemophilia - Factor VIII or IX Deficiency topic.

Featured ARUP Testing

Chromogenic Factor VIII, Activity 3002343

Method: Chromogenic Assay

- Measures hydrolysis of a p-nitroanilide (pNA) substrate
  - The rate of release of pNA is proportional to the factor VIII activity in the sample
- Can quantitate factor activity as low as 1% of normal

Disease Overview

Incidence

Hemophilia A in 1/4,000-5,000 live male births worldwide; rare in females[2,3]

Inheritance

X-linked recessive, factor VIII deficiency can also be acquired due to autoantibodies.[2,3]

Visit the Hemophilia - Factor VIII or IX Deficiency Consult topic for additional information about factor VIII deficiency.

Diagnostic Issues

Hemophilia A may be classified as mild, moderate or severe, based on factor activity.[3]

Expected Factor VIII Activity in Hemophilia A

Disease Classification	Expected Factor Activity
Mild	6-40%
Moderate	1-5%
Severe	<1%

Monitoring Issues

Modified extended half-life factor VIII replacement products may lead to under- or overestimation of factor VIII activity in clot-based factor VIII assays using certain aPTT reagents.[4,5,6] For more information about the effects of specific factor VIII replacement products on factor VIII activity, refer to the Effects of Extended Half-Life Factor VIII Replacement Products on Factor VIII Activity table.

Additionally, factor VIII activity cannot be accurately measured using a one-stage clot-based factor VIII activity assay in the presence of emicizumab.[7] Measurement of factor VIII activity or factor VIII inhibitors in the presence of emicizumab requires a chromogenic assay

using bovine reagents (either a chromogenic factor VIII activity or a chromogenic factor VIII Bethesda assay). The ARUP chromogenic factor VIII activity assay uses bovine reagents and is not affected by emicizumab.

Test Interpretation

Results

- Age-specific reference intervals are provided for each result on the patient chart.
- Decreased factor VIII activity is expected in patients with hemophilia A (refer to the Expected Factor VIII Activity in Hemophilia A table for disease classification) and is associated with increased risk of bleeding.

Limitations

- Decreased chromogenic factor VIII activity results may also be caused by:
  - von Willebrand disease
  - Specimen collection and storage issues:
    - Uncontrolled freeze-thaw cycles
    - Prolonged ambient storage
    - Activated or clotted specimens
  - Anticoagulant medications (assay interference)
    - Heparin (>2 U/mL)
    - Direct thrombin inhibitors
    - Direct Xa inhibitors
- Factor VIII activity may be elevated above usual baseline (normal or high result could mask underlying deficiency) in patients with acute phase responses.
- Normal factor VIII activity does not exclude female hemophilia carrier status.

References

1. Verbruggen B, Meijer P, Novákova I , et al. Diagnosis of factor VIII deficiency. *Haemophilia* . 2008;14 Suppl 3:76-82.

2. Fijnvandraat K, Cnossen MH, Leebeek FW , et al. Diagnosis and management of haemophilia. *BMJ* . 2012;344:e2707.

3. Srivastava A, Santagostino E, Dougall A, et al. WFH guidelines for the management of hemophilia, 3rd edition [published correction appears in *Haemophilia* . 2021;27(4):699]. *Haemophilia* . 2020;26 Suppl 6:1-158.

4. Graf L. Extended half-life factor VIII and factor IX preparations. *Transfus Med Hemother* . 2018;45(2):86-91.

5. Kitchen S, Tiefenbacher S, Gosselin R. Factor activity assays for monitoring extended half-life FVIII and factor IX replacement therapies. *Semin Thromb Hemost* . 2017;43(3):331-337.

6. St Ledger K, Feussner A, Kalina U, et al. International comparative field study evaluating the assay performance of AFSTYLA in plasma samples at clinical hemostasis laboratories. *J Thromb Haemost* . 2018;16(3):555-564.

7. Müller J, Pekrul I, Pötzsch B, et al. Laboratory monitoring in emicizumab-treated persons with hemophilia A. *Thromb Haemost* . 2019;119(9):1384-1393.