Chromogenic Factor VIII, Activity

Chromogenic factor VIII activity is used for diagnosis of mild hemophilia A (in conjunction with one-stage clot-based factor VIII activity) and measurement of factor VIII activity in the presence of interfering drugs or lupus anticoagulants that result in underestimation by clot-based methods. It is also used for measuring factor VIII activity in patients treated with certain modified extended half-life factor VIII replacement products and emicizumab.

Disease Overview

Incidence
Hemophilia A in 1/4,000-5,000 live male births worldwide; rare in females.\(^1\)

Inheritance
X-linked recessive, factor VIII deficiency can also be acquired due to autoantibodies.\(^1\)

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.

<table>
<thead>
<tr>
<th>Disease Classification</th>
<th>Expected Factor Activity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild</td>
<td>6-35%</td>
</tr>
<tr>
<td>Moderate</td>
<td>1-5%</td>
</tr>
<tr>
<td>Severe</td>
<td>&lt;1%</td>
</tr>
</tbody>
</table>

Mild hemophilia A may require both one-stage clot-based factor VIII activity and chromogenic factor VIII activity for diagnosis, due to differences in how the underlying mutations affect factor VIII activity in the tests.\(^2\)

Monitoring Issues

Modified extended half-life factor VIII replacement products may lead to underestimation of factor VIII activity in clot-based factor VIII assays using certain aPTT reagents.\(^3,4,5\)

<table>
<thead>
<tr>
<th>Extended Half-Life FVIII Replacement Product</th>
<th>Manufacturer</th>
<th>Modification Type</th>
<th>Effect on FVIII Activity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adynovate</td>
<td>Shire/Baxalta, Baxter PEGylated (random) rFVIII</td>
<td>Acceptable recovery with chromogenic or one-stage FVIII activity for all aPTT reagents tested to date Relatively higher recovery with aPTT reagents with ellagic acid activators (eg, Actin FS, Actin FSL) that is not clinically significant</td>
<td></td>
</tr>
<tr>
<td>Afstyla</td>
<td>CSL Behring</td>
<td>Single chain, B-domain truncated rFVIII</td>
<td>Underestimated with all one-stage FVIII activity assays; package insert recommends use of correction factor which is supported by a multicenter field study Acceptable recovery with chromogenic FVIII activity assays</td>
</tr>
</tbody>
</table>
Factor VIII activity cannot be accurately measured using a one-stage clot-based factor VIII activity assay in the presence of emicizumab. 6

- Emicizumab is a bispecific antibody that bridges factor IX and factor X to produce activated factor X (FXa). Emicizumab effectively replaces the function of factor VIII in secondary hemostasis
- Emicizumab will substitute for factor VIII function in one stage clot-based factor VIII activity assays and will result in overestimation of factor VIII activity (either native factor VIII or factor VIII concentrate administered in an acute care setting)
  - Interference may last for up to 6 months following end of therapy
- In patients receiving emicizumab, patient factor VIII activity (endogenous or factor VIII concentrate) can be accurately measured using chromogenic factor VIII activity with bovine reagents
  - Emicizumab can bind to factor IX and X in chromogenic assays using human factor-derived reagents and will still overestimate factor VIII activity
  - The chromogenic factor VIII activity assay at ARUP Laboratories uses bovine reagents and is not affected by emicizumab
- Measuring factor VIII inhibitors in patients receiving emicizumab requires use of a Bethesda assay based on a chromogenic factor VIII assay (bovine reagents)

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 (see table above 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


Related Information

Hemophilia - Factor VIII or IX Deficiency

Related Tests

von Willebrand Panel 0030125
Method: Electromagnetic Mechanical Clot Detection/Platelet Agglutination/Microlatex Particle-Mediated Immunoassay

Factor VIII, Activity 0030095
Method: Electromagnetic Mechanical Clot Detection

Factor VIII Activity with Reflex to Bethesda Quantitative, Factor VIII 0030026
Method: Electromagnetic Mechanical Clot Detection
