BloodCenter’s Hemophilia Testing Algorithm
An integrated, innovative suite of tests

BloodCenter’s Hemophilia testing algorithm uses a series of tests and analyses to correctly identify the disease. Our Hemophilia tests maximize patient benefit by providing a complete, patient-specific work-up that yields a highly accurate and actionable diagnosis. This approach to Hemophilia management, combined with our experienced, expert team, can only be found at BloodCenter.

There are two principle types of Hemophilia:
• Hemophilia A is caused by a reduction in the amount of the blood coagulation Factor VIII.
• Hemophilia B is caused by a reduction in the amount of the blood coagulation Factor IX.

Tests Available for Hemophilia

Factor VIII Activity: Clotting based activity assay is valuable in detecting partial or near total absence of the blood clotting protein Factor VIII. The assay is also useful in the ongoing monitoring of individuals on Factor VIII replacement therapy for a diagnosis of Hemophilia A.

Factor VIII Inhibitor Analysis: Uses the standard Bethesda assay format to identify and quantify inhibitory antibodies to the Factor VIII protein. This assay is valuable in the identification and monitoring of patients that have formed an inhibitor for Factor VIII.

Factor VIII Severe Hemophilia A Genetic Analysis: Comprehensive reflexive algorithm for the causative genetics in Severe Hemophilia A. The Factor VIII Inversion analysis is performed first and if negative for the Intron 22 and Intron 1 inversions, samples are reflexed to Factor VIII Sequence Analysis. Patients with mild or moderate Hemophilia A should proceed directly to full gene sequencing.

Factor VIII Inversion Analysis: Tests for the presence of the Intron 22 and Intron 1 inversions found in approximately 50% of Severe Hemophilia A patients.

Factor VIII Sequence Analysis: Includes bidirectional sequencing of the entire coding region of the Factor VIII gene.

Factor IX Activity: Clotting based activity assay is valuable in detecting partial or near total absence of the blood clotting protein Factor IX. The assay is also useful in the ongoing monitoring of individuals on Factor IX replacement therapy for a diagnosis of Hemophilia B.

Factor IX Inhibitor Analysis: Assay uses the standard Bethesda assay format to identify and quantify inhibitory antibodies to the Factor IX protein. This assay is valuable in the identification of and monitoring patients that have formed an inhibitor.

Factor IX Sequence Analysis: Assay includes bidirectional sequencing of the entire coding region of the Factor IX gene.

Hemophilia A Diagnosis Algorithm* 1

<table>
<thead>
<tr>
<th>Prolonged Prothrombin Time (PT)</th>
<th>Factor VIII Activity Test</th>
<th>Inversion Found?</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 1 IU/dL</td>
<td>Severe Hemophilia A</td>
<td>Yes</td>
<td>Normal</td>
</tr>
<tr>
<td>1-5 IU/dL</td>
<td>Moderate Hemophilia A</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>5-40 IU/dL</td>
<td>Mild Hemophilia A</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>&gt;40 IU/dL</td>
<td>Normal</td>
<td>-</td>
<td></td>
</tr>
</tbody>
</table>

* The Hemophilia B Diagnosis Algorithm follows the same path as Hemophilia A using the Factor IX Activity Test and Sequence Analysis, instead of Factor VIII. If a diagnosis of Severe Hemophilia B is found, the recommendation would be to progress directly to the Factor IX Sequence Analysis rather than the Inversion Analysis.