

# Bleeding Disorders

## TWO NEW PANELS FOR DIAGNOSIS OF COMMON AND UNCOMMON BLEEDING DISORDERS

### Test Highlights

- New panel for common bleeding disorders (2003417) includes testing for von Willebrand disease, factor VIII deficiency, factor IX deficiency, and factor XI deficiency.
- New panel for uncommon bleeding disorders (2003947) includes testing for factor II deficiency, factor V deficiency, factor VII deficiency, factor X deficiency, dysfibrinogenemia, and screening for factor XIII deficiency/inhibitor.

### Clinical Background

- Some inherited bleeding disorders are common, while others are markedly uncommon.
- Acquired conditions, such as vitamin K deficiency/warfarin therapy, liver disease, and disseminated intravascular coagulation, are often associated with multiple factor deficiencies.

DEFICIENCY	INCIDENCE	INHERITANCE PATTERN
von Willebrand disease	1 in 100	Autosomal dominant
Factor VIII deficiency	1 in 4,000–5,000 males	X-linked recessive
Factor IX deficiency	1 in 30,000 males	X-linked recessive
Factor XI deficiency	1 in 100,000–1 million, 1 in 200 in the Ashkenazi Jewish population	Autosomal recessive
Factor II, V, X, and XIII deficiencies	1 in 1–2 million	Autosomal recessive
Factor VII deficiency	1 in 500,000	Autosomal recessive
Dysfibrinogenemia	Unknown, but rare	Autosomal dominant

- Characteristic prothrombin time (PT) and partial thromboplastin time (PTT) patterns can help guide initial testing for inherited bleeding disorders, although exceptions do occur due to patient heterogeneity and variability in reagent sensitivity.

TYPICAL PT AND PTT RESULTS	BLEEDING DISORDER
Isolated prolonged PTT	Factor VIII, IX, and XI deficiencies, some cases of von Willebrand disease
Isolated prolonged PT	Factor VII deficiency
Prolonged PT and PTT	Factor II, factor V, and factor X deficiencies, some cases of dysfibrinogenemia
Normal PT and PTT	Many cases of von Willebrand disease, factor XIII deficiency, some cases of dysfibrinogenemia

### Indications for Ordering

- These tests are appropriate in the initial work-up of patients with a suspected bleeding disorder.
- Clinical presentation, family history, results of basic coagulation tests (e.g., PT, PTT), and mixing studies can be used to guide appropriate test selection.

- The von Willebrand tests included in the common bleeding disorders panel are the recommended first-line tests for von Willebrand disease.
  - Additional testing may be required for diagnosis and/or subtyping.

### Interpretation

Reference intervals for factor activities often differ between children and adults; age-appropriate reference intervals will be provided where applicable.

### Limitations

- The tests included in these panels will not differentiate between inherited deficiency and acquired deficiency due to an acquired autoantibody (with the exception of the factor XIII test, which is a screening test for factor XIII deficiency/inhibitor). Additional testing, such as Bethesda assays, may be indicated in certain cases.
- The factor XIII test included in the uncommon bleeding disorders panel (Factor XIII, Qualitative, with Reflex to Factor XIII 1:1 Mix) is a qualitative screening test that identifies samples with severe factor XIII deficiency (less than 1 percent of normal activity). Samples with less severe deficiency will not be identified. If clot lysis occurs in the initial testing, the test is repeated using a 1:1 mix of patient plasma and pooled normal plasma to distinguish between FXIII deficiency and a FXIII inhibitor. Quantitative factor XIII testing is recommended for confirmation of abnormal results (currently an ARUP sendout test).
- The presence of heparin may interfere with the assays for factors VIII, IX, and XI.
- The presence of a direct thrombin inhibitor may interfere with the assays for fibrinogen and factors II, V, VII, VIII, IX, X, and XI.
- Other causes of bleeding, such as qualitative platelet dysfunction and fibrinolytic abnormalities, will not be identified.

### Methodology

- Electromagnetic mechanical clot detection (fibrinogen, factors II, V, VII, VIII, IX, X, XI).
- Microlatex particle-mediated immunoassay (vWF antigen).
- Platelet agglutination (vWF activity-ristocetin cofactor activity).
- Clot solubility (factor XIII).
- Radial immunodiffusion (fibrinogen antigen).

## Related Tests

- Prothrombin Time (0030215)
- Inhibitor Assay, PT with Reflex to PT 1:1 Mix (2003260)
- Partial Thromboplastin Time (0030235)
- Inhibitor Assay, PTT with Reflex to PTT 1:1 Mix, with Reflex to 1-Hour Incubation (2003266)
- Factor VIII Activity (0030095)
- Hemophilia A (F8) 2 Inversions with Reflex to Sequencing and Reflex to Deletion/Duplication (2001614)
- Hemophilia A (F8) 2 Inversions (2001759)
- Hemophilia A (F8) 2 Inversions, Fetal (2001755)
- Hemophilia A (F8) Deletion/Duplication (2001751)
- Hemophilia A (F8) Sequencing (2001747)
- von Willebrand Factor Antigen (0030285)
- von Willebrand Factor Activity (Ristocetin Cofactor) (0030250)
- von Willebrand Panel (0030125)
- von Willebrand Multimeric Panel (0030002)

- von Willebrand Factor Multimers (0092281)
- Factor VIII Activity with Reflex to Bethesda Quantitative, Factor VIII (0030026)
- Factor IX Activity (0030100)
- Hemophilia B (F9) Sequencing (2001578)

## References

- Friedman KD, Rodgers GM. Inherited coagulation disorders. In *Wintrobe's clinical hematology*, 12th ed. Greer JP, et al, eds. 2009 Philadelphia: Lippincott Williams and Wilkins, 1379–424.
- Nichols WL, et al. Von Willebrand disease (VWD): evidence-based diagnosis and management guidelines, the National Heart, Lung, and Blood Institute (NHLBI) Expert Panel report (USA). *Haemophilia* 2008;14(2):171–232.
- Verbruggen B, et al. Diagnosis of factor VIII deficiency. *Haemophilia* 2008;14 Suppl 3:76–82.
- Hsieh L, Nugent D. Factor XIII deficiency. *Haemophilia* 2008;14:1190–1200.

## Test Information

**2003947**                    **Bleeding Disorders (Uncommon) with Reflex to Factor XIII 1:1 Mix and/or Fibrinogen Antigen**  
**2003417**                    **Bleeding Disorders (Common)**

For specific collection, transport, and testing information, refer to the ARUP website at [www.aruplab.com](http://www.aruplab.com).

For information on test selection, ordering, and interpretation, refer to ARUP Consult® at [www.arupconsult.com](http://www.arupconsult.com).