

Laboratory and Other Studies for Diagnosis of Hemophilia A and B

Test	Notes
Activated partial thromboplastin time	The aPTT is prolonged when either factor VIII or factor IX activity is 30% or less of the control plasma pool. The aPTT may also be prolonged in von Willebrand's disease or factor XI deficiency
Prothrombin time	The PT is normal in hemophilia A or B, von Willebrand's disease, or factor XI deficiency
aPTT 50/50 mixing study	A mixing study will show correction of a prolonged aPTT if the prolongation is due to a factor deficiency. Failure of the mixing study to correct a prolonged aPTT supports the presence of a coagulation factor inhibitor
Quantitative coagulation factor assays for factor VIII and factor IX	Specific quantitative coagulation factor assays should be performed to determine whether the shown deficiency is either factor VIII or factor IX. Deficiencies of other coagulation factors, such as factor XI can also be determined. The results of these studies will be reported as either percent of the normal control plasma pool activity or as a fraction of IU/mL plasma (1 IU is the normal amount of factor VIII or IX activity in 1 mL control plasma pool; therefore, 10% activity can be reported as 0.1 IU/mL)
Assays for von Willebrand's factor activity (ristocetin co-factor activity)	Patients without a family history of hemophilia A who are found to have low factor VIII activity should also be screened for von Willebrand's factor activity to exclude a diagnosis of von Willebrand's disease
Factor VIII or factor IX inhibitor assays	A failure to correct an abnormal prolonged aPTT test in a 50/50 mixing study is diagnostic of the presence of a coagulation factor inhibitor. Acquired inhibitors to factor VIII can occur as a complication of treatment of severe hemophilia A in nearly 20% of patients or occur spontaneously in older patients, patients with immune disorders or malignancies, or in postpartum women. Inhibitors against factor IX are much less frequent and occur in only 3%-4% of patients. Inhibitory activity is reported as Bethesda units with one unit of inhibitory activity capable of inhibiting 50% of factor activity in normal plasma.
Factor VIII or IX mutation determination	Mutation profiling may assist in screening for carrier status in a family and assist in future genetic counseling. Mutation profiling may also identify patients at high risk for developing inhibitors.
Complete blood count with platelet count	In an actively bleeding patient, assessment of hemoglobin level is appropriate in order to determine the need for RBC transfusion. Soft tissue bleeding, unlike hemarthrosis, can progressively advance along muscle planes and may be extensive without visible ecchymoses. Bleeding may be a manifestation of severe thrombocytopenia and this should be excluded from the differential diagnosis. Thrombocytopenia can also occur in hemophilia patients infected with HIV or hepatitis C virus
Liver function tests	Older hemophilia patients who have received multiple transfusions with blood and coagulation factors may develop chronic hepatitis with subsequent cirrhosis
Serologic studies for HIV and hepatitis B and C infections	Older hepatitis patients with a history of transfusions and plasma-derived factor replacement should be screened for infections due to blood-borne pathogens such as HIV and hepatitis B and C. Over 75% of patients with severe hemophilia and 46% of moderate hemophilia patients treated during the 1980s HIV seroconverted.
Magnetic resonance imaging of large joints and symptomatic joints	MRI evaluation of joint involvement has proven to be the most reliable imaging method to evaluate the presence and progression of hemophilia-related joint destruction.

aPTT = activated partial thromboplastin time; HIV = human immunodeficiency virus; IU = international units; MRI = magnetic resonance imaging; PT = prothrombin time; RBC = red blood cell (erythrocyte).

From *Physicians Information and Education Resource (PIER), Hemophilia module.*

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