MAYO CLINIC LABORATORIES

Test Definition: 8INHE

Factor VIII Inhibitor Evaluation, Plasma

Overview

Useful For

Detecting the presence and titer of a specific factor inhibitor directed against coagulation factor VIII

This test is **not useful** for the detection of a lupus-like circulating anticoagulant inhibitor, a nonspecific circulating anticoagulant, or other inhibitors that are not specific for coagulation factors.

Profile Information

Test Id	Reporting Name	Available Separately	Always Performed
8INHT	FVIII Inhib Profile Tech Interp	No	Yes
F8A	Coag Factor VIII Activity Assay, P	Yes	Yes

Reflex Tests

Test Id	Reporting Name	Available Separately	Always Performed
8AINH	FVIII Inhib Profile Prof Interp	No	No
8BETH	FVIII Bethesda Units, P	No	No
F8IS	Coag Factor VIII Assay Inhib Scrn,P	No	No

Testing Algorithm

Testing begins with the coagulation factor VIII activity assay with dilutions to evaluate assay inhibition; if the factor VIII activity assay is normal or increased, a technical interpretation will be provided.

If the factor VIII activity assay is decreased, an inhibitor screen to look for specific factor VIII inhibition will be performed at an additional charge and a professional interpretation will be provided. If specific inhibition is apparent, the titer of the inhibitor will be determined.

Special Instructions

- Coagulation Guidelines for Specimen Handling and Processing

Method Name

F8A, F8IS, 8BETH: Optical Clot-Based
8INHT: Technical Interpretation
8AINH: Medical Interpretation

NY State Available

Yes

Specimen

Specimen Type
Plasma Na Cit

Ordering Guidance
This test is for factor VIII inhibitors only. If the patient is known to have hemophilia A, this is the correct test to order. If the presence or type of inhibitor is unknown, first order APROL / Prolonged Clot Time Profile, Plasma. When screening studies are needed for patients with known hemophilia B, order 9INHE / Factor IX Inhibitor Evaluation, Plasma.

Shipping Instructions
Send all vials in the same shipping container.

Specimen Required
Specimen Type: Platelet-poor plasma
Patient Preparation:
1. Patient **should not** be receiving anticoagulant treatment (eg, warfarin, heparin). If not possible for medical reasons, note on request.
 a. If medically feasible, for 4 to 6 hours before specimen collection, **do not** administer intravenous heparin.
 b. If medically feasible, for 10 to 14 days before specimen collection, **do not** administer subcutaneous heparin or warfarin**.**
2. Patient **should not** be receiving fibrinolytic agents (streptokinase, urokinase, tissue plasminogen activator [tPA]).
3. It is recommended that specimens be collected pretransfusion. If patient has been transfused, **a specimen should not be collected for 48 hours.**
Collection Container/Tube: Light-blue top (3.2% sodium citrate)
Submission Container/Tube: 13-mm x 75-mm, 5-mL, plastic vial (polypropylene preferred)
Specimen Volume: 3 mL Platelet-poor plasma in 3 plastic vials, each containing 1 mL
Collection Instructions:
1. Specimen must be collected prior to factor replacement therapy.
2. For complete instructions, see Coagulation Guidelines for Specimen Handling and Processing.
3. Centrifuge, transfer all plasma into a plastic vial, and centrifuge plasma again.
4. Aliquot plasma (1-2 mL per aliquot) into 3 separate plastic vials, leaving 0.25 mL in the bottom of centrifuged vial.
5. Immediately freeze plasma (no longer than 4 hours after collection) at -20 degrees C or, ideally, at -40 degrees C or below.
Additional Information:
1. A double-centrifuged specimen is critical for accurate results as platelet contamination may cause spurious results.
2. Each coagulation assay requested should have its own vial.

Forms
If not ordering electronically, complete, print, and send a Coagulation Test Request (T753) with the specimen.

Specimen Minimum Volume

Platelet-poor plasma: 2 Plastic vials, each containing 1 mL

Reject Due To

Gross hemolysis	Reject
Gross lipemia	Reject
Gross icterus	Reject

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Plasma Na Cit	Frozen	14 days	

Clinical & Interpretive

Clinical Information

Factor VIII (FVIII) inhibitors are IgG antibodies directed against coagulation FVIII that typically result in development of potentially life-threatening hemorrhage. These antibodies may develop in 1 of 4 different patient populations:
-Patients with congenital FVIII deficiency (hemophilia A) in response to therapeutic infusions of factor VIII concentrate
-Older nonhemophiliac adult patients (not previously factor VIII deficient)
-Women in the postpartum period
-Patients with other autoimmune illnesses

Reference Values

FACTOR VIII ACTIVITY ASSAY
Adults: 55-200%
Normal, full-term infants or healthy premature infants typically have levels greater or equal to 40%.*
*See Pediatric Hemostasis References in Coagulation Guidelines for Specimen Handling and Processing.

FACTOR VIII INHIBITOR SCREEN:
Negative

GENERAL FACTOR BETHESDA UNITS:
< or =0.5 Bethesda Units

Interpretation

Normally, there is no inhibitor (ie, negative result).

If the screening assays indicate the presence of an inhibitor, it will be quantitated and reported in Bethesda (or equivalent) units.

Cautions

Occasionally, a potent lupus-like anticoagulant may cause false-positive results for a specific factor inhibitor (eg, factor

VIII or IX).

Clinical Reference

1. Hoffman R, Benz Jr EJ, Silberstein LE, et al, eds. Hematology: Basic Principles and Practice. 7th ed. Elsevier; 2018
2. Kasper CK. Treatment of factor VIII inhibitors. Prog Hemost Thromb. 1989;9:57-86
3. Peerschke EI, Castellone DD, Ledford-Kraemer M, et al. Laboratory assessment of FVIII inhibitor titer. Am J Clin Pathol. 2009;131(4):552-558. doi:10.1309/AJCPMKP94CODILWS
4. Pruthi RK, Nichols WL. Autoimmune factor VIII inhibitors. Curr Opin Hematol. 1999;6(5):314-322. doi:10.1097/00062752
5. Kottke-Marchant. K, ed. Laboratory Hematology Practice. Wiley Blackwell Publishing; 2012

Performance

Method Description

The factor VIII assay is performed on the Instrumentation Laboratory ACL TOP using the activated partial thromboplastin time (aPTT) method and a factor-deficient substrate. Patient plasma is combined and incubated with a factor VIII-deficient substrate (normal plasma depleted of factor VIII by immunoadsorption) and an aPTT reagent. After a specified incubation time, calcium is added to trigger the coagulation process in the mixture. Then the time to clot formation is measured optically using a wavelength of 671 nm.(Owen CA Jr, Bowie EJW, Thompson JH Jr. Diagnosis of Bleeding Disorders. 2nd ed. Little, Brown and Company; 1975; Cielsa B. Defects of plasma clotting factors. In: Hematology in Practice. 3rd ed. FA Davis; 2019:chap 17)

The factor VIII inhibitor screen consists of measuring the difference in factor VIII activity (partial thromboplastin time-based assay) before and after incubation of a mixture of normal plasma and patient's plasma for 1 hour at 37 degrees C. For optimal sensitivity, the factor VIII value of the normal plasma is adjusted to approximately 20%, because the factor VIII assay is more sensitive in this area of the curve. In addition, an excess of patient's plasma will make the test more sensitive to small amounts of inhibitors.(Owen CA Jr, Bowie EJW, Thompson JH Jr. The Diagnosis of Bleeding Disorders. 2nd ed. Little, Brown, and Company; 1975:143-145; Cielsa B. Defects of plasma clotting factors. In: Hematology in Practice. 3rd ed. FA Davis; 2019:chap 17)

If the inhibitor screen is positive for an inhibitor of factor VIII, the inhibitor will be quantitated by the Bethesda assay. In the Bethesda procedure, inhibitors are quantified by mixing equal volumes of serially diluted plasma with normal plasma. This mixture is incubated 2 hours at 37 degrees C, and its factor VIII activity is measured and compared to a control run at the same time. The difference between the factor VIII activity of the patient's incubation mixture and that of the control is used to calculate the titer. The residual factor VIII activity is converted to Bethesda units: 50% residual factor VIII is equal to 1 Bethesda unit. Assays using the same basic principle as the Bethesda assay are used to quantitate the inhibitors of the other coagulation factors.(Kasper CK, Aldedort LM, Counts RB, et al. A more uniform measurement of factor VIII inhibitors. Thromb Diath Haemorrh. 1975;34:869-872; Cielsa B. Defects of plasma clotting factors. In: Hematology in Practice. 3rd ed. FA Davis; 2019:chap 17)

PDF Report

No

Day(s) Performed

Monday through Friday

Report Available
1 to 3 days

Specimen Retention Time
7 days

Performing Laboratory Location
Mayo Clinic Laboratories - Rochester Main Campus

Fees & Codes

Fees
- Authorized users can sign in to Test Prices for detailed fee information.
- Clients without access to Test Prices can contact Customer Service 24 hours a day, seven days a week.
- Prospective clients should contact their account representative. For assistance, contact Customer Service.

Test Classification
This test has been modified from the manufacturer's instructions. Its performance characteristics were determined by Mayo Clinic in a manner consistent with CLIA requirements. This test has not been cleared or approved by the US Food and Drug Administration.

CPT Code Information
85390-Factor VIII Tech Interp
85240-Factor VIII activity assay
85335-Bethesda titer (if appropriate)
85335-Factor VIII inhibitor screen (if appropriate)
85390-Factor VIII Professional Interp (if appropriate)

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
8INHE	Factor VIII Inhib Profile, P	96456-9

Result ID	Test Result Name	Result LOINC® Value
F8A	Coag Factor VIII Activity Assay, P	3209-4
8INHT	FVIII Inhib Profile Tech Interp	69049-5