MAYO CLINIC LABORATORIES

# Test Definition: ALBLD

Bleeding Diathesis Profile, Limited, Plasma

## Overview

### Useful For

Detection of the more common potential causes of abnormal bleeding (eg, factor deficiencies/hemophilia, von Willebrand disease, factor-specific inhibitors) and a simple screen to evaluate for an inhibitor or severe deficiency of factor XIII (rare)

This test is **not useful for** assessing platelet function (eg, congenital or acquired disorders such as Glanzmann thrombasthenia, Bernard-Soulier syndrome, storage pool disease, myeloproliferative disease, associated platelet dysfunction), which requires fresh platelets.

### Profile Information

| Test Id | Reporting Name | Available Separately | Always Performed |
|---|---|---|---|
| ALBLI | Limited Bleed Prof Interp | No | Yes |
| PTSC | Prothrombin Time (PT), P | Yes, (order PTTP) | Yes |
| APTSC | Activated Partial Thrombopl Time, P | Yes, (order APTTP) | Yes |
| TTSC | Thrombin Time (Bovine), P | Yes | Yes |
| CLFIB | Fibrinogen, Clauss, P | Yes, (order FIBTP) | Yes |
| DIMER | D-Dimer, P | Yes, (order DDITT) | Yes |
| F8A | Coag Factor VIII Activity Assay, P | Yes | Yes |
| F_9 | Coag Factor IX Assay, P | Yes | Yes |
| FXIII | Factor XIII(13),Scrn | No | Yes |
| VWAG | von Willebrand Factor Ag, P | Yes | Yes |
| VWACT | von Willebrand Factor Activity, P | Yes | Yes |

### Reflex Tests

| Test Id | Reporting Name | Available Separately | Always Performed |
|---|---|---|---|
| GBETH | General Factor Bethesda Units, P | No | No |
| 5BETH | FV Bethesda Units, P | No | No |
| 8BETH | FVIII Bethesda Units, P | No | No |
| 9BETH | FIX Bethesda Units, P | No | No |
| F8IS | Coag Factor VIII Assay Inhib Scrn,P | No | No |
| RIST | Ristocetin Cofactor, P | No | No |
| FACTV | Coag Factor V Assay, P | Yes | No |

| | | | |
|---|---|---|---|
| F_7 | Coag Factor VII Assay, P | Yes | No |
| F_10 | Coag Factor X Assay, P | Yes | No |
| F_11 | Coag Factor XI Assay, P | Yes | No |
| F_12 | Coag Factor XII Assay, P | Yes | No |
| F_2 | Coag Factor II Assay, P | Yes | No |
| F9_IS | Factor IX Inhib Scrn | No | No |
| F5_IS | Factor V Inhib Scrn | No | No |
| F2_IS | Factor II Inhib Scrn | No | No |
| F7_IS | Factor VII Inhib Scrn | No | No |
| 10_IS | Factor X Inhib Scrn | No | No |
| 11_IS | Factor XI Inhib Scrn | No | No |
| PNP | Platelet Neutralization Procedure | No | No |
| PSGN | Plasminogen Activity, P | Yes | No |
| PAI1 | PAI-1 Ag, P | Yes | No |
| CH9 | Chromogenic FIX, P | Yes | No |
| ATTI | Antithrombin Antigen, P | Yes | No |
| ATTF | Antithrombin Activity, P | Yes | No |
| PTMSC | PT Mix 1:1 | No | No |
| APMSC | APTT Mix 1:1 | No | No |
| DRV2 | DRVVT Mix | No | No |
| DRV3 | DRVVT Confirmation | No | No |
| VWFMP | von Willebrand Factor Multimer, P | Yes, (order VWFMS) | No |
| DRV1 | Dilute Russells Viper Venom Time, P | Yes, (order DRVI1) | No |
| PTFIB | PT-Fibrinogen, P | No | No |
| SOLFM | Soluble Fibrin Monomer | No | No |
| RTSC | Reptilase Time, P | Yes | No |
| A2PI | Alpha-2 Plasmin Inhibitor, P | Yes | No |
| CHF8 | Chromogenic FVIII, P | Yes | No |
| HEXLA | HEX LA, P | No | No |

### Testing Algorithm

Initial testing includes prothrombin time (PT), activated partial thromboplastin time (aPTT), thrombin time (bovine), fibrinogen, D-dimer, coagulation factor VIII activity assay, coagulation factor IX assay, von Willebrand factor (VWF) antigen, VWF activity, factor XIII screen, and limited bleed profile interpretation.

If PT is greater than 13.9 seconds, then PT mix will be performed at an additional charge.

If aPTT is 38 seconds or more, then aPTT mix and dilute Russell's viper venom time (dRVVT) will be performed at an additional charge.

If dRVVT ratio is 1.20 or more, then dRVVT mix and dRVVT confirm will be performed at an additional charge.

If thrombin time is 25.0 seconds or more, then reptilase time will be performed at an additional charge.

If fibrinogen is less than 150 mg/dL, or clinically indicated, then PT-fibrinogen will be performed at an additional charge.

If D-dimer is greater than 500 ng/mL fibrinogen equivalent units (FEU), then soluble fibrin monomer will be performed at an additional charge.

If aPTT mix is 38 seconds or more and thrombin time is less than 35.0 seconds (no evidence of heparin), then platelet neutralization procedure will be performed at an additional charge.

If VWF activity assay is less than 55% or VWF activity:VWF antigen ratio is abnormally increased, then VWF ristocetin cofactor activity assay will be performed at an additional charge.

If VWF antigen is less than 55%, the VWF activity is less than 55%, or the VWF activity:VWF antigen ratio is abnormal, then VWF multimer analysis will be performed at an additional charge.

If appropriate, coagulation factor assays or hexagonal lupus anticoagulant will be performed, at an additional charge, to clarify significant abnormalities in the screen test results.

If factor result is below the normal range, the appropriate factor inhibitor screen may be performed along with the Bethesda titering assay, at an additional charge, if inhibitor screen is positive.

For more information see Hemophilia Testing Algorithm.

### Special Instructions

- Coagulation Guidelines for Specimen Handling and Processing
- Coagulation Patient Information
- Hemophilia Testing Algorithm
- Coagulation Profile Comparison

### Method Name

PTSC, APTSC, TTSC, FXIII, F8A, F_9 : Optical Clot-Based
VWAG, VWACT, DIMER: Latex Immunoassay (LIA)
CLFIB: Clauss

### NY State Available

Yes

## Specimen

### Specimen Type

Plasma Na Cit

## Ordering Guidance

Multiple coagulation profile tests are available. See Coagulation Profile Comparison for testing that is performed with each profile.

## Shipping Instructions

Send the 6 aliquots in the same shipping container.

## Necessary Information

1. Note if patient is currently receiving anticoagulant (eg, heparin, warfarin) treatment or any medication that could affect coagulation parameters.
2. Note if patient has been recently transfused.

## Specimen Required

**Specimen Type:** Platelet-poor plasma

**Patient Preparation:**

1. Patient **should not** be receiving anticoagulant treatment (eg, warfarin, heparin). Treatment with heparin causes false-positive results of in vitro coagulation testing for lupus anticoagulant. Warfarin treatment may impair ability to detect the more subtle varieties of lupus-like anticoagulants.
 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:** Plastic vials

**Specimen Volume:** 6 mL platelet-poor plasma in 6 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 6 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, -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

1. Coagulation Patient Information (T675)
2. If not ordering electronically, complete, print, and send a Coagulation Test Request (T753) with the specimen.

## Specimen Minimum Volume

Platelet-poor plasma: 4 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

Bleeding problems may be associated with a wide variety of coagulation abnormalities or may be due to problems not associated with coagulation (eg, trauma and surgery). A partial listing of causes follows.

-Deficiency or functional abnormality (congenital or acquired) of any of the following coagulation proteins: fibrinogen (factor I), factor II (prothrombin), factor V, factor VII, factor VIII (hemophilia A), factor IX (hemophilia B), factor X, factor XI (hemophilia C; bleeding severity not always proportionate to factor level), factor XIII (fibrin-stabilizing factor), von Willebrand factor (VWF antigen and activity), alpha-2 plasmin inhibitor, and plasminogen activator inhibitor (PAI-1; severe deficiency in rare cases). Neither alpha-2 plasmin inhibitor nor PAI-1 are included as a routine bleeding diathesis assay component, but either can be performed if indicated or requested.

-Deficiency (thrombocytopenia) or functional abnormality of platelets such as congenital (Glanzmann thrombasthenia, Bernard-Soulier syndrome, storage pool disorders, etc) and acquired (myeloproliferative disorders, uremia, drugs, etc) disorders. Platelet function abnormalities cannot be studied on mailed-in specimens.

-Specific factor inhibitors (most frequently directed against factor VIII); factor inhibitors occur in 10% to 15% of the hemophilia population and are more commonly associated with severe deficiencies of factor VIII or IX (antigen <1%). The inhibitor appears in response to transfusion therapy with factor concentrates with no correlation of occurrence and amount of therapy. Factor VIII inhibitors may occur spontaneously in the postpartum patient, with certain malignancies, in association with autoimmune disorders (eg, rheumatoid arthritis, systemic lupus erythematosus), in older adults, and for no apparent reason.

-Other acquired causes of increased bleeding include paraproteinemia; other factor-specific inhibitors, including those against factor V, factor XI; or virtually any of the coagulation proteins.

-Acute disseminated intravascular coagulation/intravascular coagulation and fibrinolysis (DIC/ICF), which is a fairly common cause of bleeding. Bleeding can also occur in patients with chronic ICF.

### Reference Values

An interpretive report will be provided.

### Interpretation

An interpretive report will be provided.

### Cautions

No significant cautionary statements

### Clinical Reference

1. Boender J, Kruip MJ, Leebeek FW. A diagnostic approach to mild bleeding disorders. J Thromb Haemost. 2016;14(8):1507-1516. doi:10.1111/jth.13368
2. Favaloro EJ, Lippi G. eds. Hemostasis and Thrombosis, Methods and Protocols. Humana Press; 2017

## Performance

### Method Description

Prothrombin time:
The prothrombin time (PT) assay is performed on the Instrumentation Laboratory ACL TOP. Patient sample is incubated and combined with a PT reagent containing recombinant human tissue factor, synthetic phospholipids, calcium chloride, polybrene, and buffer. The tissue thromboplastin-factor VII/VIIa complex activates factor X. Activated factor X (factor Xa) forms a complex with factor Va, calcium, and phospholipid to activate factor II (prothrombin) to thrombin. Thrombin then acts on fibrinogen (factor I) to form fibrin which clots, the time to clot formation is measured optically using a wavelength of 671 nm providing the assay endpoint (the "prothrombin time").(Package insert: HemosIL RecombiPlasTin 2G. Instrumentation Laboratory Company; R0, 03/2019)

Activated partial thromboplastin time:
The activated partial thromboplastin time (aPTT) assay is performed on the Instrumentation Laboratory ACL TOP. Patient sample is combined and incubated with an aPTT reagent containing phospholipid, a negatively charged contact factor activator, and buffer. After a specified incubation time, calcium is added to trigger the coagulation process in the mixture. Subsequently, the time to clot formation is measured optically using a wavelength of 671 nm. Mixing studies (see APMSC / Activated Partial Thromboplastin Time (APTT) Mix 1:1, Plasma) using normal pooled plasma are performed on samples with a prolonged aPTT to assist in discriminating between factor deficiency states and coagulation inhibitors unless further testing is not indicated.(Package insert: HemosIL SynthASil. Instrumentation Laboratory Company; R11, 06/2017)

Thrombin time:
The thrombin time assay is performed on the Instrumentation Laboratory ACL TOP. Patient sample is combined with a bovine thrombin reagent containing bovine albumin, calcium chloride, and buffer immediately triggering the coagulation process in the mixture. Time to clot formation is measured optically using a wavelength of 671 nm.(Package insert: HemosIL Thrombin Time. Instrumentation Laboratory Company; R1, 12/2018)

Fibrinogen, Clauss assay:
The Clauss fibrinogen assay is performed using the HemosIL Fibrinogen-C kit on the Instrumentation Laboratory ACL TOP. Patient sample, containing fibrinogen, is mixed with reagent containing excess thrombin. The excess thrombin converts the fibrinogen in the patient sample to fibrin. The amount of time it takes to form a clot is inversely proportional to the amount of fibrinogen present in the patient sample.(Package insert: HemosIL Fibrinogen-C. Instrumentation Laboratory Company; R7, 06/2017)

D-Dimer:

The D-dimer assay is performed using the HemosIL D-Dimer HS 500 kit on the Instrumentation Laboratory ACL TOP instrument. D-dimer is assayed in plasma by adding polystyrene latex particles coated with monoclonal antibodies specific for D-dimer domain. The latex particles agglutinate in the presence of soluble fibrin degradation products containing the D-dimer domain. The degree of agglutination is directly proportional to the concentration of D-dimer in the sample and is determined by measuring the decrease of transmitted light caused by the aggregates (turbidimetric immunoassay).(Package insert: HemosIL D-Dimer HS 500. Instrumentation Laboratory Company; R6, 12/2024)

Factor VIII activity:
The factor VIII assay is performed on the Instrumentation Laboratory ACL TOP using the aPTT method and a factor-deficient substrate. Patient sample 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 at 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)

Factor IX activity:
The factor IX assay is performed on the Instrumentation Laboratory ACL TOP using the aPTT method and a factor-deficient substrate. Patient sample is combined and incubated with a factor IX-deficient substrate (normal plasma depleted of factor IX 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 at 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)

Factor XIII:
The covalent stabilization of fibrin by thrombin-activated factor XIII (XIIIa) is the final event in the coagulation of blood. Plasma factor XIII (fibrin-stabilizing factor) zymogen consists of 2 "A" and 2 "B" subunits, the "A" subunits containing an active-center sulfydryl grouping mediating the transamidase activity of the enzyme. The action of thrombin converts fibrinogen to fibrin monomer causing the monomeric molecules to polymerize and be held together by noncovalent hydrogen bonds. These bonds can be broken by 5 M urea or weak acid solutions in the absence of factor XIII. Subsequent to fibrin polymerization by hydrogen bonding, the action of factor XIII results in the formation of covalent bonds that cannot be broken by 5 M urea or weak acid solutions as used in this procedure (1% monochloroacetic acid). Dissolution of a clot by urea or monochloroacetic acid is therefore a qualitative test for factor XIII activity.(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)

von Willebrand factor antigen:
This assay is performed using the HemosIL von Willebrand Factor (VWF) Antigen kit on the Instrumentation Laboratory ACL TOP. This is a latex immunoassay method using microlatex particles coated with specific rabbit-polyclonal antibody directed against VWF. In the presence of VWF antigen, antibody-coated latex particles agglutinate to form aggregates of diameters greater than the wavelength of the light passing through the sample and more light is absorbed as aggregation increases. The increase in absorption is proportional to the concentration of VWF antigen present in the sample.(Package insert: HemosIL von Willebrand Factor Antigen. Instrumentation Laboratory; R11, 05/2018)

VWF activity:

This assay is performed using the HemosIL von Willebrand Factor Activity kit on the Instrumentation Laboratory ACL TOP. This is a latex particle-enhanced immunoassay to quantify VWF activity in plasma. The activity of VWF is determined by measuring the increase of turbidity produced by the agglutination of the latex reagent. A specific anti-VWF monoclonal antibody adsorbed onto the latex reagent, directed against the platelet-binding site of VWF (glycoprotein Ib receptor), reacts with the VWF of patient sample. The degree of agglutination is directly proportional to the activity of VWF in the sample and is determined by measuring the decrease of transmitted light caused by the aggregates.(Package insert: HemosIL von Willebrand Factor Activity. Instrumentation Laboratory; R7, 05/2018)

### PDF Report
No

### Day(s) Performed
Monday through Friday

### Report Available
7 to 21 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
See Individual Test IDs

### CPT Code Information
85610-PTSC
85730-APTSC
85670-TTSC
85384-CLFIB
85379-DIMER
85390-26-ALBLI
85240-F8A
85250-F_9
85291-FXIII
85246-VWAG

85397-VWACT
85130-Chromogenic factor VIII (if appropriate)
85130-Chromogenic factor IX (if appropriate)
85210-Factor II (if appropriate)
85220-Factor V (if appropriate)
85230-Factor VII (if appropriate)
85245-Ristocetin cofactor (if appropriate)
85247-von Willebrand factor multimer (if appropriate)
85260-Factor X (if appropriate)
85270-Factor XI (if appropriate)
85280-Factor XII (if appropriate)
85300-Antithrombin activity (if appropriate)
85301-Antithrombin antigen (if appropriate)
85335-Bethesda units (if appropriate)
85335-Factor II inhibitor screen (if appropriate)
85335-Factor V inhibitor screen (if appropriate)
85335-Factor VII Inhibitor screen (if appropriate)
85335-Factor VIII inhibitor screen (if appropriate)
85335-Factor IX inhibitor screen (if appropriate)
85335-Factor X inhibitor screen (if appropriate)
85335-Factor XI inhibitor screen (if appropriate)
85366-Soluble fibrin monomer (if appropriate)
85385-PT-Fibrinogen (if appropriate)
85410-Alpha-2 plasmin inhibitor (if appropriate)
85415-PAI-1 Ag (if appropriate)
85420-Plasminogen Activity (if appropriate)
85597-Platelet neutralization for lupus inhibitor (if appropriate)
85598-Hex LA (if appropriate)
85611-PT mix 1:1 (if appropriate)
85613-DRVVT (if appropriate)
85613-DRVVT mix (if appropriate)
85613-DRVVT confirm (if appropriate)
85635-Reptilase time (if appropriate)
85732-APTT mix 1:1 (if appropriate)