Overview

Useful For

Evaluating patients with thrombosis or hypercoagulability states

Detecting a lupus-like anticoagulant; dysfibrinogenemia; disseminated intravascular coagulation/intravascular coagulation and fibrinolysis

Detecting a deficiency of antithrombin, protein C, or protein S

Detecting activated protein C resistance (and the factor V R506Q [Leiden] mutation if indicated)

Detecting the prothrombin G20210A mutation

Profile Information

Test ID	Reporting Name	Available Separately	Always Performed
AATHI	Thrombophilia Interpretation	No	Yes
PTSC	Prothrombin Time (PT), P	Yes, (order PTTP)	Yes
APTSC	Activated Partial Thrombopl Time, P	Yes, (order APTTP)	Yes
DRV1	Dilute Russells Viper Venom Time, P	Yes, (order DRVI1)	Yes
TTSC	Thrombin Time (Bovine), P	Yes	Yes
CLFIB	Fibrinogen, Clauss, P	Yes, (order FIBTP)	Yes
DIMER	D-Dimer, P	Yes, (order DDITT)	Yes
ATTF	Antithrombin Activity, P	Yes	Yes
CFX	Protein C Activity, P	Yes	Yes
PSF	Protein S Ag, Free, P	Yes, (order PSTF)	Yes
APCRV	Activated Protein Resistance V, P	Yes	Yes
PTNT	Prothrombin G20210A Mutation, B	Yes	Yes

Reflex Tests

Test ID	Reporting Name	Available Separately	Always Performed
IBETH	Bethesda Units	No	No
F8IS	Coag Factor VIII Assay Inhib Scrn,P	No	No
ATTI	Antithrombin Antigen, P	Yes	No
FACTV	Coag Factor V Assay, P	Yes	No

Test ID	Reporting Name	Available Separately	Always Performed
F_7	Coag Factor VII Assay, P	Yes	No
F_9	Coag Factor IX 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
F8A	Coag Factor VIII Activity Assay, P	Yes	No
RTSC	Reptilase Time, P	Yes	No
F_2	Coag Factor II Assay, P	Yes	No
PCAG	Protein C Ag, P	Yes	No
F5DNA	Factor V Leiden (R506Q) Mutation, B	Yes	No
PNP	Platelet Neutralization Procedure	No	No
PTMSC	PT Mix 1:1	No	No
APMSC	APTT Mix 1:1	No	No
PST	Protein S Ag, Total, P	No	No
STACL	Staclot LA, P	No	No
DRV2	DRVVT Mix	No	No
DRV3	DRVVT Confirmation	No	No
S_FX	Protein S Activity, P	Yes	No
SOLFM	Soluble Fibrin Monomer	No	No
PTFIB	PT-Fibrinogen, P	No	No

Testing Algorithm

Initial testing includes: prothrombin time (PT); activated partial thromboplastin time (APTT); dilute Russell viper venom time (DRVVT); thrombin time (bovine); fibrinogen; D-dimer; antithrombin activity; protein C activity; protein S antigen, free; prothrombin G20210A mutation; activated protein resistance V; and thrombophilia interpretation.

If PT is >13.9 seconds, PT mix will be performed at an additional charge.

If APTT is > or =38 seconds, APTT mix will be performed at an additional charge.

If APTT mix is > or =38 seconds and thrombin time is <35.0 seconds (no evidence of heparin), platelet neutralization procedure will be performed at an additional charge.

If DRVVT ratio is > or =1.20, DRVVT mix and DRVVT confirmation will be performed at an additional charge.

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

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

If D-dimer is >500 ng/mL FEU, soluble fibrin monomer will be performed at an additional charge.

If protein S antigen, free is <65% for males and females > or =50 years of age and <50% for females <50 years of age, protein S antigen, total will be performed at an additional charge.

If protein C activity is <70% with no evidence for an acquired decrease in protein C activity, protein C antigen may be performed at an additional charge.

If antithrombin activity is <80% with no evidence of an acquired decrease in antithrombin activity, antithrombin antigen will be performed at an additional charge.

If activated protein C resistance (APC) ratio is <2.3 or baseline APC APTT is prolonged, factor V leiden (R506Q) mutation analysis will be performed at an additional charge.

If appropriate, protein S activity, coagulation factor assays, or Staclot LA will be performed at an additional charge to clarify significant abnormalities in the screen test results.

If factor VIII result is <55%, the factor VIII inhibitor screen may be performed along with the Bethesda titering assay, if inhibitor screen is positive.

See Thrombophilia Profile in Special Instructions.

Special Instructions

- Coagulation Guidelines for Specimen Handling and Processing
- Informed Consent for Genetic Testing
- Coagulation Patient Information
- Thrombophilia Profile
- Informed Consent for Genetic Testing (Spanish)
- Coagulation Profile Comparison

Method Name

PTSC, APTSC, DRV1, TTSC, APCRV: Optical Clot-Based

CLFIB: Clauss

DIMER, PSF,: Latex Immunoassay (LIA)

ATTF, CFX: Chromogenic Assay

PTNT: Direct Mutation Analysis

NY State Available

Yes

Specimen

Specimen Type

Plasma Na Cit
Whole blood

Advisory Information

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

Shipping Instructions

Send all specimens in the same shipping container.

Specimen Required

See Coagulation Guidelines for Specimen Handling and Processing in Special Instructions.

Both blood and plasma are required.

Specimen Type: Whole blood

Container/Tube:

Preferred: Yellow top (ACD)

Acceptable: EDTA, sodium citrate

Specimen Volume: 6 mL

Collection Instructions:

1. Invert several times to mix blood.

2. Do not transfer blood to other containers.

3. Label specimen as whole blood.

Patient Preparation:

1. Patient should not be receiving Coumadin, heparin, direct thrombin inhibitors (argatroban, dabigatran), or direct factor Xa inhibitors (apixaban, rivaroxaban, and edoxaban).

2. Specimen must be drawn prior to initiation of anticoagulants and thrombolytic therapy.

Specimen Type: Platelet-poor plasma

Collection Container/Tube: Light-blue top (citrate)

Submission Container/Tube: Polypropylene vials

Specimen Volume: 5 mL in 5 Polypropylene vials each containing 1 mL

Collection Instructions:

1. Spin down, remove plasma, and spin plasma again.

2. Freeze plasma immediately (no longer than 4 hours after collection) at -20 degrees C or, ideally< or = -40 degrees C, .

3. Label specimens as plasma.

Additional Information:

1. Double-centrifuged specimen is critical for accurate results as platelet contamination may cause spurious results.

2. If priority specimen, mark request form, give reason, and request a call-back.

Forms

1. **New York Clients-Informed consent is required.** Document on the request form or electronic order that a copy is on file. The following documents are available in Special Instructions:

-Informed Consent for Genetic Testing (T576)

-Informed Consent for Genetic Testing-Spanish (T826)

2. Coagulation Patient Information (T675) in Special Instructions

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

Specimen Minimum Volume

Whole Blood: 3 mL
Plasma: 5 mL in 5 polypropylene 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	
Whole blood	Ambient (preferred)	7 days	
	Frozen	14 days	
	Refrigerated	14 days	

Clinical and Interpretive

Clinical Information

Thrombophilia is defined as an acquired or familial disorder associated with thrombosis. The clinical presentation of an underlying thrombophilia predominantly includes venous thromboembolism (deep vein thrombosis, pulmonary embolism, superficial vein thrombosis). Other manifestations that have been linked to thrombophilia include recurrent miscarriage and complications of pregnancy (eg, severe preeclampsia, abruptio placentae, intrauterine growth restriction, stillbirth). The current thrombophilia does not predict for arterial thrombosis. Demographic or environmental exposures that compound the risk of venous thromboembolism among persons with a thrombophilia include increasing age, male gender, obesity, surgery, trauma, hospitalization for medical illness, malignant neoplasm, prolonged immobility during travel (eg, prolonged airplane travel), oral contraceptive use, estrogen

therapy (both oral and transdermal), tamoxifen and raloxifene therapy, and infertility drugs. Central venous catheters and transvenous pacemaker wires increase the risk for upper extremity deep vein thrombosis; this risk is unrelated to thrombophilia.

Inherited thrombophilias include:

-Deficiency due to reduced plasma protein level or dysfunctional protein of:

Â -Antithrombin

Â -Protein C

Â -Protein S

-Dysfibrinogenemias (rare)

-Activated protein C resistance due to the factor V R506Q (Leiden) mutation

-Prothrombin G20210A mutation

Acquired thrombophilias include a lupus-like anticoagulant (antiphospholipid antibodies) and disseminated intravascular coagulation/intravascular coagulation and fibrinolysis (DIC/ICF). DIC/ICF may cause thrombotic as well as hemorrhagic events. Positive tests for DIC/ICF can also occur as consequences of thrombosis.

Acquired deficiencies of fibrinogen, protein C, protein S, and antithrombin may be found in conjunction with liver disease (they are produced by the liver) or DIC/ICF and are of uncertain significance with respect to thrombosis risk.

Acquired deficiencies of protein C and protein S are also found in patients with liver disease who are being treated with oral anticoagulants (eg, warfarin, Coumadin), since both of these proteins are dependent upon the action of vitamin K for normal function.

Acquired protein S deficiency also occurs in thrombotic thrombocytopenic purpura, pregnancy or estrogen therapy, nephrotic syndrome, and sickle cell anemia. In acute illness, the level of acute-phase reactants rise (including C4b binding protein, which binds and inactivates protein S in the plasma) and the portion of bound protein S also rises leaving a lower proportion of free protein S. The significance of acquired protein S deficiency with respect to thrombosis risk is unknown.

Reference Values

An interpretive report will be provided.

Interpretation

An interpretive report will be provided.

Cautions

To obtain the most useful information, this testing is best performed in medically-stable patients who are not receiving oral vitamin K inhibitor (eg, warfarin, Coumadin), heparin, low-molecular-weight heparin, hirudin (Refludan), argatroban, fibrinolytic agents (eg, streptokinase, tissue plasminogen activator), or platelet GPIIbIIIa (alpha IIb beta3) inhibitors (abxicimab [ReoPro], tirofiban, aggrastat). However, useful information can be obtained in patients receiving anticoagulation therapy.

Clinical Reference

1. Pengo V, Tripodi A, Reber G, et al: Update of the guidelines for lupus anticoagulant detection. Subcommittee on

Lupus Anticoagulant/Antiphospholipid Antibody of the Scientific and Standardization Committee of the International Society on Thrombosis and Haemostasis. J Thromb Haemost 2009;7(10):1737-1740

2. Keeling D, Mackie I, Moore GW, et al: Guidelines on the investigation and management of antiphospholipid syndrome. Br J Haemotol 2012;157(1):47-58

3. Clinical and Laboratory Standards Institute (CLSI). Laboratory Testing for the Lupus Anticoagulant; Approved Guideline. CLSI document H60-A. Wayne, PA, Clinical Laboratory Standards Institute, 2014

Performance

Method Description

PTC: Optical clot-based

Tissue thromboplastin (phospholipid and recombinantly-derived human tissue factor) and calcium are added to citrated plasma, bypassing the action of platelets and factors VIII, IX, XI, and XII in the intrinsic procoagulant pathway. 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, providing the assay endpoint (the "prothrombin time").(Package insert: HemosIL RecombiPlasTin 2G Instrumentation Laboratory Company, Lexington, MA, R0, 9/2007)

APTSC: Optical clot-based

The activated partial thromboplastin time (APTT) assay is performed on the Beckman Coulter ACL TOP. Patient plasma 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 APTTM / APTT Mix 1:1) using normal pooled plasma are performed in the Special Coagulation

Laboratory on samples with a prolonged APTT, to assist in discriminating between factor deficiency states and coagulation inhibitors, unless further testing is not indicated.(Poller L: Activated partial thromboplastin time (APTT). In Laboratory Techniques in Thrombosis; A Manual. Edited by J Jesperson, RM Bertina, F Haverkate. Dordrecht and London, Kluwer Academic Publishers, 1999, pp 337-343)

RVR1: Optical clot-based

The dilute Russell viper venom time (DRVVT) screening assay is performed on the Instrumentation Laboratory ACL TOP. Patient plasma is incubated for a specified time, and then combined with a DRVVT screening reagent containing Russell viper venom, phospholipids, heparin neutralizing agents, calcium, buffers and stabilizers to trigger the coagulation process. Subsequently, the time to clot formation is measured optically using a wavelength of 671 nm. The patient DRVVT screening clotting time is normalized by dividing the patient result by the mean DRVVT screening clotting time of normal pooled plasma to yield a ratio (DRVVT screen ratio).(Package insert: LA CHECK DRVVT Precision Biologic, Dartmouth, Nova Scotia, Canada. March 2012)

TTSC: Optical clot-based

The thrombin time (TT) assay is performed on the Instrumentation Laboratory ACL TOP. Patient plasma 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 405 nm.(Package insert: HemosIL Thrombin Time, Instrumentation Laboratory Company, Bedford, MA. Revision 10/2011)

CLFIB: Clauss assay

The Clauss fibrinogen assay is performed using the HemosIL Fibrinogen-C kit on the Instrumentation Laboratory ACL TOP. Patient plasma, containing fibrinogen, is mixed with reagent containing excess thrombin. The excess thrombin converts the fibrinogen in the patient plasma to fibrin. The amount of time it takes to form a clot is inversely proportional to the amount of fibrinogen present in the patient plasma.(Clauss A: Rapid physiological coagulation method in determination of fibrinogen. Acta Haematol 1957;17:237-246; Rossi E, Mondonico P, Lombardi A, Preda L: Method for the determination of functional [clottable] fibrinogen by the new family of ACL coagulometers. Thromb Res 1988;52:453-468; Hollensead SC, Triplett DA: Review of fibrinogen methods: clinical considerations. ASCP Check Specimen: 10[4] 1988 [TH 88-4]; Palareti G, Maccaferri M, Manotti C, et al: Fibrinogen assays: a collaborative study of six different methods. Clin Chem 1991;37:714-719)

DIMER: Latex immunoassay (LIA)

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 (FDP) 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, Bedford, MA 2/2017)

ATTF: Chromogenic

This assay is performed using the HemosIL Liquid Antithrombin Kit on the Instrumentation Laboratory ACL TOP instrument. Patient plasma, containing antithrombin, is mixed and incubated with reagent containing factor Xa and excess heparin. Factor Xa activity in the reagent is rapidly inhibited by antithrombin. Residual factor Xa activity is then measured using an amidolytic activity assay. This occurs when residual factor Xa lyses chromogenic substrate S-2765 (N-alpha-Z-D-Arg-Gly-Arg-pNA 2HCI) and subsequently releases pNA (detected at 405 nm) in a level that is inversely proportional to the amount of antithrombin in the sample. This method is based on inhibition of factor Xa and, therefore, only higher amounts of heparin cofactor II, alpha-2-macroglobulin, or alpha-1-antitrypsin will influence the assay.(Package insert: HemosIL Liquid Antithrombin. Instrumentation Laboratory Company, Bedford, MA, Rev 6 08/2014)

CFX: Chromogenic

This assay is performed using the HemosIL Protein C kit on the Beckman Coulter ACL TOP. Protein C in plasma is activated by a specific enzyme (Protein C activator) from copperhead snake venom (Agkistrodon contortrix contortrix). The amount of activated protein C is determined by the rate of hydrolysis of the chromogenic substrate, S-2366 (pyroGlu Pro-Arg-pNA-HCL). The pNA release is measured kinetically at 405 nm and is directly proportional to the protein C level in the plasma.(Package insert: HemosIL Protein C, Instrumentation Laboratory, Bedford, MA, 12/2008)

PSF: Latex Immunoassay (LIA)

This assay is performed using the HemosIL Free Protein S kit on the Beckman Coulter ACL TOP. The assay uses latex immunoassay methodology to determine the presence of free protein S. It consists of 2 latex reagents, one being latex particles coated with purified human C4BP and the other is latex particles coated with a monoclonal antibody directed against human protein S. Patient plasma is combined with the purified C4BP that reacts with a high affinity for free protein S in the patient plasma. The free protein S adsorbed on the C4BP latex triggers the agglutination reaction with the second latex reagent. The aggregates form diameters greater than the wavelength of the light (405nm) passing through, causing absorption of the light. This change in absorption is measured over time and reported as delta optical density (OD). The increase in absorption is proportional to the concentration of free

protein S antigen present in the patient plasma.

APCRV: Optical clot-based

This assay is performed using the HemosIL Factor V Leiden (APC Resistance V) Kit on the ACL TOP instrument. The method uses a modified activated partial thromboplastin time (APTT) test to detect activated protein C (APC) resistance. The plasma specimen is prediluted in factor V-deficient plasma. Then the APTT test is performed by incubating patient plasma with a standardized amount of platelet-like phospholipids and activator of the contact factors of the intrinsic coagulation pathway, followed by recalcification of plasma and measurement of clotting time. The ratio of the APTT test with and without added APC is reported as the APC resistance (or sensitivity) ratio.(Package insert: HemosIL Factor V Leiden [APC Resistance V]. Instrumentation Laboratory Company, Bedford, MA, Rev 10/2012)

PTNT: Direct Mutation Analysis

Direct mutation analysis using PCR amplification, signal generation, and release by cleavage of sequence specific alleles.(Invader Factor II, Invader Plus Chemistry, Hologic, Madison, WI)

PDF Report

No

Day(s) and Time(s) Test Performed

Monday through Friday

Analytic Time

4-7 days

Specimen Retention Time

7 days for plasma, 1 month for whole blood

Performing Laboratory Location

Rochester

Fees and 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 Regional Manager. For assistance, contact Customer Service.

Test Classification

See Individual Test IDs

CPT Code Information

81240-*F2* (prothrombin, coagulation factor II) (eg, hereditary hypercoagulability) gene analysis, 20210G->A variant

85300-AT activity

85303-Protein C activity

85306-Protein S antigen, free

85307-Activated protein resistance V

85379-D-Dimer

85384-Fibrinogen

85390-26-Special coagulation interpretation

85610-PT

85613-DRVVT

85670-Thrombin time

85730-APTT

81241-F5 (coagulation factor V) (eg, hereditary hypercoagulability) gene analysis, Leiden variant (if appropriate)

85210-Factor II (if appropriate)

85220-Factor V (if appropriate)

85230-Factor VII (if appropriate)

85240-Factor VIII (if appropriate)

85250-Factor IX (if appropriate)

85260-Factor X (if appropriate)

85270-Factor XI (if appropriate)

85280-Factor XII (if appropriate)

85301-Antithrombin antigen (if appropriate)

85302-Protein C antigen (if appropriate)

85305-Protein S antigen, total (if appropriate)

85306-Protein S activity (if appropriate)

85335-Bethesda titer (if appropriate)

85335-Factor VIII inhibitor screen (if appropriate)

85366-Soluble fibrin monomer (if appropriate)

85385-PT-Fibrinogen (if appropriate)

85597-Platelet neutralization for lupus inhibitor (if appropriate)

85598-Staclot LA (if appropriate)

85611-PT mix 1:1 (if appropriate)

85613-DRVVT mix (if appropriate)

85613-DRVVT confirmation (if appropriate)

85635-Reptilase time (if appropriate)

85732-APTT mix 1:1 (if appropriate)

LOINC® Information

Test ID	Test Order Name	Order LOINC Value
AATHR	Thrombophilia Prof	In Process

Result ID	Test Result Name	Result LOINC Value
CLFIB	Fibrinogen, Clauss, P	48664-7
603184	Thrombophilia Interpretation	69049-5
603325	Reviewed by	18771-6
RVR1	DRVVT Screen Ratio	15359-3
21803	Prothrombin G20210A Mutation, B	24475-6
APTSC	Activated Partial Thrombopl Time, P	75506-6
PTSEC	Prothrombin Time (PT), P	5902-2
TTSC	Thrombin Time (Bovine), P	46717-5
DIMER	D-Dimer, P	48067-3
ATTF	Antithrombin Activity, P	27811-9
CFX	Protein C Activity, P	27818-4
PSF	Protein S Ag, Free, P	27821-8
APCR	APCRV Ratio	13590-5
INT55	Interpretation	48591-2
INRSC	INR	6301-6
21804	PTNT Interpretation	69049-5
21806	PTNT Reviewed By	18771-6