Cleveland Clinic Laboratories
Quality | Service | Experience

Hemostasis and Thrombosis Consultative Group
How to Contact the Cleveland Clinic Hemostasis and Thrombosis Consultative Group

For more information about Hemostasis and Thrombosis Services at Cleveland Clinic Laboratories, please contact:

**Technical Information**
Lynne Manteuffel, MT(ASCP)
*Manager, Hematology Laboratory*
216.444.0483 | manteul@ccf.org

Tim Paustian, MT(ASCP)
*Lab Coordinator, Hemostasis and Thrombosis*
216.445.1862 | paustit@ccf.org

**Scientific Information**
Kandice Kottke-Marchant, MD, PhD
*Section Head, Hemostasis and Thrombosis*
216.444.2484 | marchak@ccf.org

**Customer Service**
216.444.5755 | 800.628.6816 (toll-free) | 216.444.0460 (Fax)
ClientServices@ccf.org

**Submit specimens to:**
Cleveland Clinic Laboratories
2119 E. 93rd Street
Cleveland OH 44106

Complete information about tests, specimen preparation and ordering is available at [www.clevelandcliniclabs.com](http://www.clevelandcliniclabs.com)

David Bosler, MD, *Head*, Cleveland Clinic Laboratories
Raymond Tubbs, DO, *Medical Director*, Cleveland Clinic Laboratories

On the Cover: Transmission electron micrograph of platelets from a patient with a congenital macrothrombocytopenia.
Cleveland Clinic

Hemostasis and Thrombosis Consultative Group

Cleveland Clinic Laboratories offers comprehensive testing for the evaluation of patients with inherited and acquired bleeding disorders, platelet dysfunction, thromboembolic complications, hypercoagulable states and anticoagulant monitoring.

Why Choose the Cleveland Clinic Hemostasis and Thrombosis Consultative Group?

We emphasize quality, state-of-the-art testing, expert pathologist interpretation, customer service, and competitive pricing.

Hemostasis disorders often are clinically puzzling, and laboratory testing in hemostasis is a rapidly changing field. Our staff of experienced pathologists can recommend appropriate laboratory testing for evaluation of patients with bleeding or thrombotic symptoms. We offer expert interpretation of laboratory results, integrating the patient’s medical and drug history, as well as recommendations for further evaluation of patients with hemostasis disorders.

Our extensive quality control assures safe, protected and expedited handling for each specimen to protect the quality of the results.

Cleveland Clinic Laboratories is accredited by the College of American Pathologists, certified by the CLIA and Medicare approved.
Specialized Diagnostic and Consultative Services

To evaluate patients with recurrent thrombosis, Cleveland Clinic Laboratories offer a well defined array of testing for inherited and acquired abnormalities related to the hypercoagulable state. Our comprehensive testing and interpretative capabilities aid in diagnosing and planning appropriate intervention for these patients.

For patients with suspected congenital or acquired bleeding disorders, such as von Willebrand disease or hemophilia, we offer consultation by a pathologist with expertise in designing appropriate laboratory approaches for evaluation of coagulation, fibrinolytic and platelet function for pinpointing these difficult-to-diagnose problems.

In addition to a complete range of diagnostic testing services, we also offer monitoring services for patients on anticoagulants, such as heparin or warfarin. We offer testing to screen for resistance to antiplatelet drugs, such as aspirin or clopidogrel. Our staff is experienced in evaluating bleeding disorders in patients on anticoagulation therapy and in designing a diagnostic approach for evaluating the cause of heparin resistance.

In consultation with the referring physician, our pathologists can develop a customized testing plan to meet the needs of the patient with a complex or unusual hemostasis disorder.
Hemostasis Testing Services

Inherited Bleeding Disorders

Hemophilia A and B
- Diagnostic testing
- Acquired coagulation inhibitors to factor VIII and IX
- Testing for other acquired coagulation inhibitors available on request

von Willebrand disease (including subtype analysis)
- Diagnostic testing
- DDAVP stimulation tests

Other bleeding disorders
- Factor deficiencies
- Hypofibrinogenemia
- Dysfibrinogenemia

Fibrinolytic bleeding disorders

Monitoring factor replacement therapy

Acquired Bleeding Disorders

Acquired factor inhibitors: detection and titer
- Antibody cross-reactivity with Porcine factor VIII
Disseminated intravascular coagulation

Vitamin K deficiency
Super-warfarin poisoning
Liver disease

Platelet Dysfunction

Acquired disorders
- Drug effect
- Myeloproliferative disorders

Congenital disorders
- Glanzmann’s thrombasthenia
- Bernard-Soulier syndrome
- Platelet storage pool disorders

Hypercoagulable State and Thromboembolic Disorders

Defects and deficiencies of natural anticoagulants
- Antithrombin
- Protein C
- Protein S

Activated protein C resistance
- Functional assays and molecular diagnosis of factor V Leiden gene mutation

Hypofibrinolytic disorders

Multilevel testing for lupus anticoagulants and antiphospholipid antibodies

Hyperhomocysteinemia
- Mutation analysis for methylene tetrahydrofolate reductase (MTHFR)

Hypofibrinogenia

Dysfibrinogenenia

Heparin-induced thrombocytopenia (HIT)

Thrombotic thrombocytopenic purpura (TTP)

Molecular testing for prothrombin G20210A mutation
**Core Laboratory Services**

In addition to our traditional reference laboratory services, we offer complete core laboratory services for large, multicenter hemostasis research studies and clinical trials. Our experience in this area includes site coordination, protocol development, sample kit design and preparation, assay performance, database entry and data analysis.

**Research**

Research in the evaluation and development of state-of-the-art techniques and instrumentation to enhance the diagnosis of hemostasis disorders is constantly in progress.

Our research focuses on the development of new diagnostic laboratory tests for monitoring antiplatelet drugs, study of genetic risk factors for thrombosis and antiplatelet drug resistance, diagnostic assays for heparin-induced thrombocytopenia, and platelet flow cytometric techniques for diagnosing platelet dysfunction and activation. We are also involved in clinical trials of new antithrombotic agents, hemostatic evaluation of patients with artificial organs, and basic research to investigate the biocompatibility of biomaterials.
Continuing Education

Hemostasis and Thrombosis lectures and educational programs are available for your professional and technical staff as requested.

For more information on continuing education programs or a complete list of lecture topics available through Cleveland Clinic Laboratories, please contact Client Services at 216.444.5755 or 800.628.6816.
## Assays to Detect Bleeding Disorders

### Coagulation Screening Assays
- Prothrombin Time (PT)/International Normalized Ratio (INR)
- Activated Partial Thromboplastin Time (APTT)
- Thrombin Time (TT)
- PT Mixing Studies
- APTT Incubated Mixing Study

### von Willebrand Assays
- Factor VIII Activity
- von Willebrand Factor Antigen
- Ristocetin Cofactor
- Collagen Binding Assay
- Ristocetin Aggregation*
- von Willebrand Multimer Assay
- Exon 28 Sequencing
- Von Willebrand Propeptide Antigen

### Coagulation Factor Assays
- Fibrinogen clottable (Clauss)
- Fibrinogen Antigen – Immunologic
- Reptilase
- Factor II Activity
- Factor V Activity
- Factor VII Activity
- Factor VIII Activity
- Factor IX Activity
- Factor X Activity
- Factor XI Activity
- Factor XII Activity
- Prekallikrein Activity
- Factor XIII (Clot solubility)

### Factor XII Quantity Assays
- Mixing Studies (PT and APTT)
- Bethesda Inhibitor Assay
  (Available to factor VIII, porcine factor VIII, factor IX, other factors as needed)

### Fibrinolytic Evaluation
- Fibrinogen clottable (Clauss)
- Fibrinogen antigen – Immunologic
- Plasminogen activity – Chromogenic
- Plasminogen Antigen – Immunologic
- Alpha 2 Plasmin Inhibitor
- Fibrin/Fibrinogen Degradation Products
- D-dimer (Quantitative immunoassay)
- Euglobulin Lysis Time

### Disseminated Intravascular Coagulation
- PT
- APTT
- Fibrinogen clottable (Clauss)
- D-dimer (Quantitative immunoassay)
- Antithrombin activity

### Vitamin K Deficiency
- Factor II Activity
- Factor V Activity
- Factor VII Activity
- Factor IX Activity
- Factor X Activity

### Hepatic Coagulopathy
- Fibrinogen clottable (Clauss)
- Fibrinogen Antigen – Immunologic
- Reptilase
- Factor II Activity
- Factor V Activity
- Factor VII Activity
- Factor VIII Activity
- Factor IX Activity
- Factor X Activity
- Factor XI Activity
- Factor XII Activity
- D-dimer (Quantitative immunoassay)
Assays to Detect Hypercoagulable Disorders

- Protein C Assay – Chromogenic
- Protein C Antigen
- Protein S – Clottable
- Protein S Immunologic (total & free)
- Activated Protein C Resistance
- Factor V Leiden (by PCR)
- Prothrombin G20210A Gene mutation by PCR
- MTHFRC677T Gene mutation by PCR
- Antithrombin assay – Chromogenic
- Antithrombin antigen
- Plasminogen antigen
- Homocysteine, plasma (HPLC)

**Lupus Anticoagulant and Antiphospholipid Antibody Testing**
- APTT Mixing Study
- Dilute Russell's Viper Venom Time (DRVVT)

- Hexagonal Phase Phospholipid Neutralization Assay (STACLOT)
- Platelet Neutralization Procedure (PNP)
- Anticardiolipin Antibody Assay (IgG, IgM, IgA)
- Anti β2-GP1 Antibody Assay (IgG and IgM)

**Heparin-Platelet Antibody Testing**
- Heparin-Antiplatelet Factor 4 IgG ELISA
- Platelet Antibody/heparin – by heparin induced platelet aggregation (HIPA)

**Thrombotic Thrombocytopenic Purpura (TTP Testing)**
- ADAMTS 13 activity
- ADAMTS 13 inhibitor

Platelet Function Assays

- Platelet Count
- Platelet Aggregation (ADP, Epinephrine, Collagen, Arachidonic Acid, Ristocetin, Luminescent ATP dense granule release)*
- Platelet function screening test by PFA-100*

- Platelet Flow cytometry* (Platelet surface analysis for fibrinogen receptor (GPIIb/IIIa), von Willebrand factor receptor (GPIb/IX), Collagen receptor (GPIa/IIa), Assessment of platelet granules and platelet release (mepacrine uptake/release and CD62 expression)

* Available to local clients only
Anticoagulation and Antiplatelet Monitoring

- Heparin assay (by Factor Xa inhibition method)
- Low molecular weight heparin assay (by Factor Xa inhibition method)
- Aspirin and clopidogrel resistance by platelet aggregation*
- Warfarin level (HPLC)
- Brodifacoum level (for super-warfarin detection)
- Fondaparinux assay (by Factor Xa inhibition method)

Other Testing Available

- Reptilase Time
- Lipoprotein (a)
- Viscosity, serum
- Viscosity, plasma

A variety of testing is available for research purposes. Please contact Dr. Kandice Kottke-Marchant at 216.444.2484 for specific test availability.

* Available to local clients only
** These Assays are for Research Only
Panels

These panels are available to evaluate patients with complex hemostatic problems.

Components of these panels may be ordered separately, if not all tests are necessary given a patient's condition.

**Lupus Anticoagulant Panel**
PT, APTT, Incubated APTT mixing study, Dilute Russell’s Viper Venom Time (DRVVT), Hexagonal Phase Phospholipid Neutralization (STACLOT), Platelet Neutralization procedure (PNP), Anticardiolipin Antibodies (IgG, IgM, IgA), Anti β2-GP1 Antibody Assay (IgG and IgM)

**Hypercoagulation Panel**
PT, APTT, Hexagonal Phase Phospholipid Neutralization (STACLOT), Fibrinogen, Anticardiolipin Antibodies (IgG, IgM, IgA), Factor VIII activity, C Reactive Protein, Antithrombin activity, Protein C activity, Protein S clottable, APC-resistance, plasma Homocysteine and Prothrombin G20210A mutation. Incubated APTT mixing study, DRVVT, PNP, β2 Glycoprotein 1 antibody, Protein S Antigen, Protein C antigen and Factor V Leiden mutation performed, if needed.

**von Willebrand Panel**
PT, APTT, factor VIII activity, von Willebrand factor antigen, Ristocetin Cofactor, Collagen Binding assay and Ristocetin aggregation*. Additionally, von Willebrand factor multimer analysis and Exon 28 sequencing are performed if needed.

**Fibrinolysis Panel**
PT, APTT, Fibrinogen, Plasminogen Activity, Alpha-2 Plasmin Inhibitor, D-dimer, Fibrin/Fibrinogen Degradation products

* Available to local clients only
Blood Collection to Obtain Platelet Poor Plasma

For most coagulation tests and factor assays, use the following instructions. For individual requirements, refer to specific tests.

Obtain venous blood by drawing a clearing tube prior to obtaining the specimen. Draw the specimen in a light blue top sodium citrate tube using 3.2% buffered sodium citrate. Avoid stasis and contamination of the specimen by tissue thromboplastin.

Mix blood with anticoagulant (3.2% buffered sodium citrate) by gentle inversion. Use 0.5 ml sodium citrate for every 4.5 ml blood. An exact ratio of 9 parts blood to 1 part anticoagulant should be maintained.

Note: *If the hematocrit of the sample is ≥ 55%, the anticoagulant ratio will not be maintained and spuriously elevated PT and APTT values will be seen. Contact the laboratory for instructions on how to draw these patients.*

Centrifuge the specimen at 2500 x g for 15 minutes. Hemolyzed specimens may be rejected.

Immediately remove 2 ml (min: 1 ml) platelet-poor plasma from the red cells using a plastic pipette. Place the plasma into a properly labeled plastic vial. Glass vials will not be accepted. Freeze immediately. Freezing at -70°C is recommended. Each assay requested must be submitted in a labeled, separate plastic vial. Transport frozen on dry ice.
Technical Considerations in Hemostasis and Thrombosis Testing

For most coagulation tests, it is crucial that testing be performed on platelet poor plasma, with a platelet count of <10,000/µl. In order to produce valid results for coagulation tests and factor assays, specimen integrity is crucial and must be maintained. Specimens should be frozen within 4 hours of phlebotomy. Short draw samples (Vacutainer less than 2/3 full) are not acceptable. Some assays may be performed on a priority basis if a medical emergency exists. Contact Customer Service to make arrangements. All requests for coagulation assays should include a brief patient history and other pertinent clinical information (i.e., medications, blood products, etc.). The Hemostasis and Thrombosis Patient Information form must be filled out and submitted with the specimen.
Hemostasis and Thrombosis Staff Directory

Kandice Kottke-Marchant, MD, PhD
Chair, Pathology & Laboratory Medicine Institute
Clinical Pathology
Section Head, Hemostasis and Thrombosis
Board Certifications:
Hematology, Anatomic Pathology, Clinical Pathology
Specialty Interests:
Hemostasis and thrombosis, hematopathology
Phone: 216.444.2484
Email: marchak@ccf.org

Joyce Heesun Rogers, MD, PhD
Board Certifications:
Anatomic Pathology, Clinical Pathology
Specialty Interests:
Hemostasis, cytogenetics
Phone: 216.445.2719
Email: Rogersj5@ccf.org

Karl Theil, MD
Clinical Pathology
Board Certifications:
Hematology, Anatomic Pathology, Clinical Pathology
Specialty Interests:
Hematopathology, bone marrow transplantation, cytogenetics
Phone: 216.444.1086
Email: theilk@ccf.org

Suzanne Bakdash, MD
Clinical Pathology
Section of Transfusion Medicine
Board Certifications:
Blood Banking/Transfusion Medicine, Anatomic Pathology, Clinical Pathology
Specialty Interests:
Hemostasis and thrombosis, transfusion medicine
Phone: 216.444.4616
Email: bakdass@ccf.org
Our Mission

The Pathology & Laboratory Medicine Institute contributes to excellent patient care by providing comprehensive, high quality laboratory testing and patient-focused expert consultation. This mission is supported by innovative research and new test development, exceptional customer service, continuous quality improvement and leadership in education.

Our Vision

We will provide the highest quality laboratory testing and expert pathology diagnosis to patients institutionally, regionally and nationally.

Our Values

Clinical excellence — we provide comprehensive and high quality laboratory testing in a patient-responsive manner.

Expert diagnosis — diagnoses are provided by subspecialty experts, and consultation with physicians is important for patient care.

Continuous quality improvement — we are continuously evaluating and implementing the best practices in laboratory testing across the testing spectrum.

Dedication to our staff — our staff are our most valuable resource and are supported and recognized for their accomplishments.

Innovative test development — a continual focus on new test development is important to provide the best capabilities for patient diagnosis.

Research and education — research is crucial for leadership in laboratory medicine; education and development are important at all levels.
The Cleveland Clinic Foundation is an independent, not-for-profit, multispecialty academic medical center. It is dedicated to providing quality specialized care and includes an outpatient clinic, a hospital with more than 1,000 available beds, an education division and a research institute.

© The Cleveland Clinic Foundation 2011