



Manual: Laboratory Guide

Category: Provision of Care

Subject: **COAGULATION TESTING GUIDELINES AND MONITORING ANTICOAGULATION**

Purpose: Provide guidelines for physicians ordering diagnostic or monitoring coagulation testing.

Guidelines: **TESTS FOR ORAL ANTICOAGULANT THERAPY, E.G., WARFARIN (COUMADIN®)**

- INR: The recommended therapeutic target for most patients and patients with Lupus inhibitor is 2-3. In patients with recurrent thromboembolic events with therapeutic INR or with additional risk factors INR of 2.5-3.5 is suggested.

TESTS FOR UNFRACTIONATED HEPARIN THERAPY

- Activated Partial Thromboplastin Time (aPTT)
- Heparin Xa Level should be used instead of aPTT in the following situations:
 1. Heparin resistance
 2. Baseline aPTT prolonged by lupus anticoagulant, contact factor deficiency or oral anticoagulant therapy

The target range for heparin therapy is:

- “High dose” protocol (for deep vein thrombosis and pulmonary embolism):
aPTT: 60-101 seconds; Anti-Xa: 0.3-0.7 IU/mL.
- “Low dose” protocol (for AMI, post-thrombolytics, unstable angina, prosthetic valve):
aPTT: 45-65 seconds; Anti-Xa: 0.15-0.35 IU/mL.

TESTS FOR LOW MOLECULAR WEIGHT HEPARIN

Monitoring is not necessary in most cases. Monitor with Heparin Xa level only if one of the following indications are met:

1. Patients with renal insufficiency
2. Women during pregnancy
3. Children and newborn infants
4. Patients being treated over a prolonged period
5. Patients who are either markedly obese (>150 kg) or have low body weight

Heparin Xa level target range (if sample is collected 4 hours post dose):
0.6-1.0 IU/mL if administered twice daily, or
1.0-2.0 IU/mL if administered daily.

TESTING FOR DIRECT THROMBIN INHIBITORS (e.g., lepirudin* (Refludan®), argatroban)

- Activated Partial Thromboplastin Time (aPTT). A target range for anticoagulation with direct thrombin inhibitors is approximately 1.5-2.5 times the baseline aPTT.
- Ecarin (a venom from the *Echis carinatus* snake) clotting time.
 - Lepirudin Therapeutic Range: 50 - 90 seconds.
 - Argatroban Therapeutic Range: 110 - 280 seconds.

TESTING FOR Xa INHIBITOR Arixtra (Fondaparinux)

- Anti Xa assay used with Arixtra Standard line. To measure the peak plasma level, the sample should be collected 3-4 hours post drug administration. Recommended ranges are: Prophylactic peak plasma level: 0.3-0.5 mg/L; Therapeutic peak plasma level: 0.8-1.2 mg/L

HYPERCOAGULABLE STATES

D-Dimer is a specific marker of the breakdown of a cross-linked fibrin clot (i.e., fibrinolysis), and an indirect marker of clot formation. D-Dimer levels will be elevated after clot formation and lysis in a wide variety of conditions known to be associated with activation of coagulation, such as surgery, trauma, hematoma, pregnancy, pre-DIC conditions and DIC, etc.

Laboratory Guide

Coagulation Testing Guidelines

After venous thromboembolism (VTE), including deep vein thrombosis (DVT) and pulmonary embolism (PE) D-dimer levels are elevated. With a high sensitivity and negative predictive value for DVT, a negative D-Dimer of less than 0.6 ug/mL in conjunction with a negative venous compression ultrasonography (CUS) reliably excludes the diagnosis of DVT, thereby obviating the need for serial CUS testing.

Do not collect specimens for a hypercoagulable work-up following an acute thrombotic event or after heparin therapy is started (except genetic analysis). For an optimal diagnostic workup, specimens should be collected from patients who are off warfarin for 10-14 days; for Protein S, off warfarin for 30 days.

Testing is recommended in step-wise fashion using different levels. If all the tests in one level are negative, proceeding to higher level is recommended.

Level 1

- Lupus anticoagulant workup
- Anticardiolipin Antibody: IgG and IgM
- Glycoprotein I Antibody: IgG and IgM
- Activated Protein C Resistance or Factor V Leiden Mutation (to identify homozygous carrier)
- Prothrombin 20210 Mutation
- Antinuclear Antibody (FANA)

Level 2

- Antithrombin III, Chromogenic
- Protein C, Chromogenic
- Protein S Antigen, free
- Protein S activity, if free antigen is normal
- Fibrinogen activity (Clauss)
- Fibrinogen antigen, if activity is low

BLEEDING ABNORMALITIES

Do not collect diagnostic specimens during an acute event, e.g., in post-op setting as coagulation factors and von Willebrand complex may not be an accurate indicator of basal coagulation status.

Level 1

- Von Willebrand Disease Screen: VW Antigen, Ristocetin Cofactor Activity, Factor VIII level; von Willebrand multimers for sub-typing
- Factor IX and XI Levels
- Fibrinogen activity (Clauss)
- Fibrinogen Antigen, if activity is low
- TSH- if VW Antigen is low

Level 2

- Factor XIII
- Alpha-2 Antiplasmin

Level 3

Must schedule with Coag Lab 273-4797.

- Platelet Aggregation
- Ristocetin Induced Platelet Aggregation (RIPA)

TESTS FOR ACTIVATION OF THE COAGULATION SYSTEM

D-Dimer

Prothrombin Fragments 1.2

TESTS FOR DISSEMINATED INTRAVASCULAR COAGULATION (DIC)

Serial measurements of INR, aPTT, Fibrinogen, Platelet Count, and D-Dimer. Thromboelastograph to detect increased fibrinolysis.

Notes:

- *Refer to the individual test listings in the Laboratory Guide for the appropriate reference ranges.*
- **Contact the Coagulation Laboratory at (612) 273-4797 (or 1-800-888-8642, ext. 3-4797) for assistance with ordering and consultation.**

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