

## SAINT FRANCIS LABORATORY COAGULATION UPDATE

The Saint Francis Hospital Clinical Laboratory is pleased to announce a major expansion of coagulation testing services. With the Ulticare upgrade on March 25, 2003, we will begin using new coagulation instrumentation and more sensitive reagents, as well as offering many tests in house that were previously only available as reference tests.

### **SIGNIFICANT CHANGES IN COAGULATION TESTING EVERY PHYSICIAN SHOULD READ**

#### **Reference Ranges (effective 3/25/2003)**

<b>PT</b>	<b>9.9 - 13.6 seconds</b>
<b>INR Therapeutic Ranges (remain the same)</b>	
	<b>2.0 - 2.5      prophylaxis including high risk surgery</b>
	<b>2.0 - 3.0      deep venous thrombosis, pulmonary embolism, atrial fibrillation or bioprosthetic heart valves</b>
	<b>3.0 - 3.5      mechanical heart valve or recurrent embolism</b>
<b>PTT</b>	<b>24.1- 36.3 seconds</b>
<b>PTT Therapeutic Range for patients on unfractionated (standard) heparin</b>	
	<b>51.0 - 84.0 seconds</b>
<b>Fibrinogen</b>	<b>238 - 491 mg/dL</b>
<b>D-dimer</b>	<b>&lt;230 ng/mL normal</b>
	<b>≥230 ng/mL suspicious for thrombotic event</b>
	<b>&gt;500 ng/mL suggests DIC</b>

#### **Additional Important Information**

- **PT/INR** – The new PT/INR reagent is much more sensitive. Consequently, the PT reference and therapeutic ranges in seconds will be noticeably higher than with the old reagent system. Please use the INR when monitoring anticoagulant effect, as this will remain constant between the two reagents. **If you have previously used a sliding scale for Warfarin (Coumadin) therapy based on PT seconds, IT WILL NO LONGER BE VALID.** If your sliding scale was previously validated for use with the INR, then it may still be appropriate, but revalidation is recommended before use.
- **Fibrinogen** – A different method will be used to determine fibrinogen levels. Please be aware of the new reference range as this will be significantly different from the previous one.
- **D-dimer** - Previously the lab offered two separate methods for determination of D-dimer - a qualitative test used to screen for DIC and a quantitative test used to screen for DVT/PE. There will now be only one quantitative test which can be used accurately in both settings. Please note the interpretive guidelines included with each D-dimer test result. One benefit of this new method should be a noticeable decrease in turn-around-time. **In the setting of a possible DVT/PE, the new quantitative D-dimer has a high negative predictive value** (i.e., a negative result is useful in excluding a DVT/PE). A positive D-dimer result  $\geq 230$  is compatible with a thrombotic event, but should not be used to “rule in” a DVT/PE, as there are many additional clinical settings in which there can be

a positive D-dimer result in this range. **A D-dimer value >500 has a high positive predictive value for DIC**, but should still be interpreted in the appropriate clinical context.

- **Platelet Function Analysis (PFA)** - This test utilizes a new technology to evaluate platelet function. The initial screening test uses Collagen/Epinephrine to assess the ability of platelets to activate and aggregate. If this initial test is abnormal, then a reflex test using Collagen/ADP is performed. This test should replace the bleeding time as a screening test for bleeding disorders such as von Willebrand disease, intrinsic platelet defects, and acquired platelet defects secondary to medication effect. In the majority of cases, it will distinguish an intrinsic defect from medication effect. However, **this test may not be interpretable if the patient is thrombocytopenic (platelet count <140K) or anemic (Hct <30% ) as both of these conditions can prolong the closure time.** In the preoperative setting, if a patient has no known history of bleeding, no family history of bleeding, and has not received any anticoagulant therapy or anti-platelet medication, then no coagulation screening is suggested. **In the ABSENCE of a bleeding history or anti-platelet medication use, neither the bleeding time (BT) or platelet function analysis (PFA) is a useful predictor of surgical bleeding.** PFA Reference Range:

Collagen/Epinephrine    74 – 176 seconds

Collagen/ADP                51 – 117 seconds

- **Specific Factor Level Assays** - Individual factor assays have previously been performed 24 hours/day. In an effort to optimize coagulation services, specific factor assays will no longer be routinely performed evenings or weekends. In addition, the lab will require that either the PT or PTT be abnormally prolonged (whichever is appropriate) prior to performing a specific factor assay. Information on the sensitivity of our PT and PTT tests to various coagulation factors is available upon request. If emergent circumstances arise, please contact the coagulation laboratory to arrange STAT testing if appropriate.
- **Heparin Xa Assay** - This test will now be performed in the SFH laboratory and will be available on a 24 hour basis. Appropriate indications for this test include therapeutic monitoring of LMW heparin and evaluation of anticoagulant therapy in patients with a lupus anticoagulant or specific factor inhibitor that artifactually increases the PTT.

### **Monitoring LMW Heparin Therapy (enoxaparin-Lovenox, dalteparin-Fragmin)**

#### *How do you monitor LMW Heparin anticoagulation?*

- **THE PT and PTT are not useful for monitoring LMW Heparin**
- Anti-Factor Xa level is the **ONLY** reliable way to monitor LMW Heparin
- Heparin Xa Assay should be drawn 4 hours after the 2<sup>nd</sup> or 3<sup>rd</sup> dose and the drug specified (There are separate curves for each drug)

#### *Which patients receiving LMW heparin should be monitored using the anti-Xa assay?*

- **Not every patient requires therapeutic monitoring!** In fact, most patients do not require any monitoring.
- **Comorbid conditions that increase bleeding risk should be monitored** - Renal failure (CrCl < 30 mL/min), recent or impending surgical procedures, trauma, ischemic stroke, or history of GI bleeding
- **Monitoring may be warranted for patients receiving recent or concurrent anticoagulants if clinical judgement indicates a high bleeding risk** - Aspirin, Warfarin (Coumadin), Ticlopidine (Ticlid), Clopidogrel (Plavix), Thrombolytics (Activase, Retavase), Gp IIb/IIIa antagonists (ReoPro, Integrilin), and NSAIDS (Ibuprofen, ketorolac, etc.)
- **Large or Obese Patients** - The upper limits of dosing have not been well established. Patients weighing up to 150 kg have been included in trials that used 1 mg/kg Q12 hr and 1.5 mg/kg Q24 hr dosing regimens

- **Pregnant Patients and Children** - Optimal dosage has not been established, therefore, if LMW heparin is used, anti-Xa monitoring is warranted.

What is the therapeutic range for anti-Factor Xa when monitoring LMW Heparin?

- The mechanism of action for all heparins is to enhance the ability of Antithrombin to proteolytically inactivate activated Factor X (Factor Xa).
- Thus the higher the dose of heparin, the lower the level of Factor Xa
- This inverse relationship is calculated and converted to anti-Xa units
- Although no prospective therapeutic range trials were performed and recommendations remain controversial, the generally accepted therapeutic range for anti-Xa is:

**When weight-adjusted doses are used for treatment:**

**0.5-1.1 Unit/mL for patients dosed BID**

**1.0-2.0 Unit/mL for patients dosed QD**

**When fixed doses are used for prophylaxis:**

**0.2-0.6 Unit/mL for patients dosed QD or BID**

**Values below the therapeutic range suggest inadequate LMW Heparin effect for anticoagulation**

**Values above the therapeutic range suggest over-anticoagulation**

How do you reverse over-anticoagulation with LMW Heparin?

- Enoxaparin (Lovenox) - Only **partial** reversal possible. Give 1 mg Protamine IV for every 1 mg of enoxaparin. May repeat in 2-4 hours if needed at a dose of 0.5 mg Protamine for every 1mg of enoxaparin
- Dalteparin (Fragmin) - Only **partial** reversal possible. Give 1 mg Protamine IV per 100 IU of dalteparin. May repeat in 2-4 hours, if needed at a dose of 0.5 mg per 100 IU of dalteparin

**Referral Testing to be Offered In House**

- **Lupus Anticoagulant Testing** - This will now be offered in 2 ways. The Lupus Anticoagulant Profile will include a standard DRVVT screen (Dilute Russel viper venom test) with a reflex confirmatory test if the screen is positive, as well as a sensitive PTT (a different reagent from our standard PTT) with reflex to a mixing study if the sensitive PTT is prolonged and a pathologist's interpretation. As there is no one "perfect test" that will pick up all lupus anticoagulants, the advantage of performing both tests together is a higher sensitivity, as well as explaining the etiology of a prolonged PTT in the absence of a lupus anticoagulant. Other causes of a prolonged PTT's include factor deficiencies as well as specific factor inhibitors (most commonly against Factor VIII). The DRVVT screen and confirmatory tests may still be ordered separately, apart from the lupus anticoagulant profile, as it has been done in the past.
- **Hypercoagulation Testing-** Later this spring, the lab will offer a Hypercoagulation Profile to evaluate for both hereditary and acquired causes of thrombophilia. The tests included in this profile include Protein C, Protein S, Activated Protein C-Resistance (a functional test for Factor V Leiden), Antithrombin, the previously described Lupus Anticoagulant tests, and a pathologist's interpretation. This profile will include most of the more common causes of thrombophilia. Again, these tests may still be ordered individually, but have been offered as a profile to facilitate a comprehensive and cost-effective approach to evaluation of the hypercoagulable patient.

If you have any questions regarding our new tests, or would like assistance in determining what special coagulation testing is appropriate in the evaluation of a particular coagulation disorder, please contact the Coagulation Laboratory at 494-6554, or Dr. Virginia Burdine,

Medical Director of the Hematology and Coagulation Laboratories at 494-1420. A coagulation consult is now available as an orderable test in Ulticare for physicians who want assistance with appropriate testing.