Laboratory Monitoring of Unfractionated Heparin Therapy

On November 18, 2015, the Thrombosis and Hemostasis Laboratory transitioned from the aPTT to the Heparin Level –UFH Test (PRISM Order Code: LAB317, SQ order code HEPUFH) as a means to monitor therapeutic levels of heparin anticoagulation for patients on the adult medicine heparin infusion protocol. Today, December 16, CRRT (Dialysis) and Surgery/Interventional Radiology order sets will also transition to this monitoring method. The HEPUFH test utilizes the same methodology as the low molecular weight heparin level and the Fondaparinux level.

The HEPUFH has many advantages over the aPTT clot-based method. The HEPUFH assay is unaffected by procoagulant factor concentrations, lupus anticoagulants, and/or biological variables know to impact the aPTT assay. Additionally, patients monitored by the HEPUFH method often reach therapeutic levels sooner, are more stable in the therapeutic range, require fewer dosing changes, and often receive less heparin while on therapy. Though the HEPUFH test does cost more than the aPTT test, the reduced effort to maintain therapeutic levels offsets the increased assay cost.

The therapeutic unfractionated heparin level is 0.3 to 0.7 IU/mL. This therapeutic range will remain constant and does not require any modification with reagent lot changes in the laboratory.

Initial heparin therapy monitoring should occur every 6 hours. Once the patient has reached a therapeutic HEPUFH level (0.3 to 0.7 IU/mL), monitoring can be extended to every 24 hours so long as the HEPUFH level remains therapeutic and the patient remains clinically stable. Once the heparin therapy is stopped, the UFH level must be discontinued.

The HEPUFH test is offered 24/7 in our laboratory and is only available as a stat test. Please note, as with all heparin monitoring, the specimen must be tested within 1 hour of collection. The collect time must be accurate to ensure the...
specimen is suitable for testing. Because the assay detects any source of heparin, proper specimen collection (e.g. flushing heparinized lines) is critical.

All the unfractionated heparin protocols identified in PRISM were reviewed, and the appropriate updates to the laboratory monitoring are complete. In addition, the heparin dosing regimens in these protocols were modified to reflect monitoring by HEPUFH test. Any unapproved protocols utilizing the aPTT to monitor heparin therapy must be discarded.

Unfractionated heparin exerts an anticoagulant effect by potentiating the action of the serine protease inhibitor antithrombin (AT). The HEPUFH assay relies on patient AT function, and the laboratory does not add exogenous antithrombin to the test system. Should a patient’s HEPUFH level remain sub-therapeutic following appropriate dosing with unfractionated heparin, consider evaluating the patient for AT deficiency.

The aPTT will be available as a diagnostic tool. If a clinical situation warrants further investigation for a coagulopathy (e.g. factor deficiency, lupus anticoagulant, etc.), please consult hematology and the laboratory for assistance in utilizing screening coagulation studies in a patient on heparin therapy.

Please contact Dr. Andrew Goodwin, Medical Director of the Thrombosis and Hemostasis Laboratory at The University of Vermont Medical Center, with any questions. This improvement in testing required the efforts of a multidisciplinary team including Maria Airoldi and Wes McMillan in Pharmacy, Dr. Neil Zakai in Hematology, Dr. Ray Keller and Clement Ng in PRISM, and Russell Brown, Kristin Lundy, and Dr. Lauren Pearson in Laboratory Medicine.

REFERENCES:


Rosborough TK. Monitoring Unfractionated Heparin Therapy with Anti factor Xa Activity Results in Fewer Monitoring Tests and Dosage Changes than Monitoring with the Activated Partial Thromboplastin Time. Pharmacoconomics. 1999; 19(6): 760-766.
Unfractionated Heparin Therapy
Frequently Asked Questions

Starting this past November, the laboratory assay for monitoring unfractionated heparin transitioned from the aPTT to the Unfractionated Heparin Level (UFH). Below are some common questions surrounding this transition.

Q1. When is this change going to happen?

The first phase began on Wednesday, November 18, 2015, and during this transition, pharmacy converted all patients on the adult medicine heparin infusion protocol to the updated adult medicine heparin infusion protocol.

The CRRT (dialysis) protocol and surgery/interventional radiology order sets continued to use the aPTT for monitoring. These order sets transitioned to the UFH level on December 16, 2015.

Q2. Why is UVMMC making this change in monitoring the unfractionated heparin?

This was a multidisciplinary decision which included input from hematology, pharmacy, and the laboratory. Advantages of using this test for monitoring include:

- Shorter time to reach therapeutic range
- Increased time in therapeutic range
- Fewer blood tests to monitor heparin
- Fewer heparin dose adjustments
- Limited interference by common co-morbid conditions
- No requirement to obtain a baseline UFH level prior to starting therapy
- Same assay methodology for monitoring low molecular weight heparin and fondaparinux levels
- Fully automated assay available 24/7 in the UVMMC Laboratory
- No need to modify heparin dosing treatment protocols with new reagent lot changes in the laboratory
- No significant difference in overall cost for appropriately managing a patient on unfractionated heparin
Q3. How do I order an unfractionated heparin level?
   a. The unfractionated heparin level is available using the Test ID HEPUFH.
   b. This test is only available as a stat test because the specimen must be processed within 1 hour of collection.
   c. If there is a significant delay (greater than 1 hour) between collection and processing, the specimen will be rejected and a new sample will be requested.

Q4. What is the therapeutic range and critical value unfractionated heparin infusions?
   a. The therapeutic heparin range is 0.3-0.7 IU/ml.
   b. The critical level is greater than 1.0 IU/ml.

Q5. Why might the heparin level be critically high?
   Elevated heparin levels are due to supra-therapeutic heparin in sample. Check the following to confirm result accurately reflects the patient's unfractionated heparin level:
   1. Blood sample obtained from a non-heparinized line and/or line was properly flushed.
   2. Collection site was distal to heparin infusion.
   3. Concentration of heparin infusion is correct.
   4. Infusion rate of heparin is correct.

Q6. Have the heparin infusion protocols been updated to reflect this change in testing?
   Yes, PRISM and pharmacy identified all protocols which included unfractionated heparin therapy. The clinical owners of these protocols were included in changes for monitoring and dosing unfractionated heparin. The first phase will occurred with the adult medicine heparin protocol on Wednesday, November 18. The remaining protocols went live on December 16.

Q7. Does this assay detect heparin induced thrombocytopenia (HIT)?
   No, this assay only detects the presence of heparin. A baseline hemagram and then every other day hemagram is necessary to aid in the monitoring of heparin induced thrombocytopenia (HIT). Every other day hemagram monitoring may be stopped after 15 days of continuous therapy.

Q8. Should a baseline unfractioned heparin level be measured prior to initiation of therapeutic heparin?
   No, a baseline level is often not required so long as the patient has not received any other heparin medications or direct Xa inhibitor medications (e.g. rivaroxaban, apixaban, edoxaban).
Q9. Should a baseline aPTT or PT/INR be drawn prior to initiation of therapeutic heparin?

Baseline coagulation studies are useful in the diagnostic work-up of a patient with a coagulopathy. Unless the patient has a history of a thrombotic or hemostatic disorder, these screening assays are not required when monitoring heparin therapy. If there is a clinical indication (i.e. factor deficiency, lupus anticoagulant, etc.), baseline coagulation studies should be considered. If the patient has already received heparin, please contact the laboratory to discuss appropriate diagnostic testing.

Q10. What specimen collection tube is used for measuring the unfractionated heparin level?

The unfractionated heparin level must be collected in a blue top (sodium citrate) tube filled to the appropriate volume (as indicated by the black triangle on the label).

Q11. How long after initiating UFH can an accurate steady state heparin level be drawn?

As with the aPTT, steady state is achieved 6 hours following an UFH bolus dose and infusion initiation. This is in the current protocol and will not change.

Q12. How often should heparin levels be ordered while a patient is on therapeutic heparin?

Frequency of monitoring will depend on the heparin level which is outlined in the heparin protocols. The UFH level MUST BE DISCONTINUED once the unfractionated heparin therapy is stopped.

Q13. Is the unfractionated heparin level the appropriate test for monitoring IV direct thrombin inhibitors?

No, the aPTT is the correct method for monitoring IV direct thrombin inhibitor therapy (e.g. argatroban, bivalirudin, etc.).

Q14. Is there any change to how Low Molecular Weight Heparin levels should be ordered?

No, continue to order using the low molecular weight heparin assay (Test ID HEPLMW, PRISM Code: LAB316).

Q15. Who should I contact with questions?

The following individuals are available via Provider Access Services: 847-2700
Maria Airoldi (Pharmacy)
Wes McMillian (Pharmacy)
Clem Ng (PRISM)
Ray Keller (PRISM)
Neil Zakai (Hematology)
Andrew Goodwin (Laboratory)