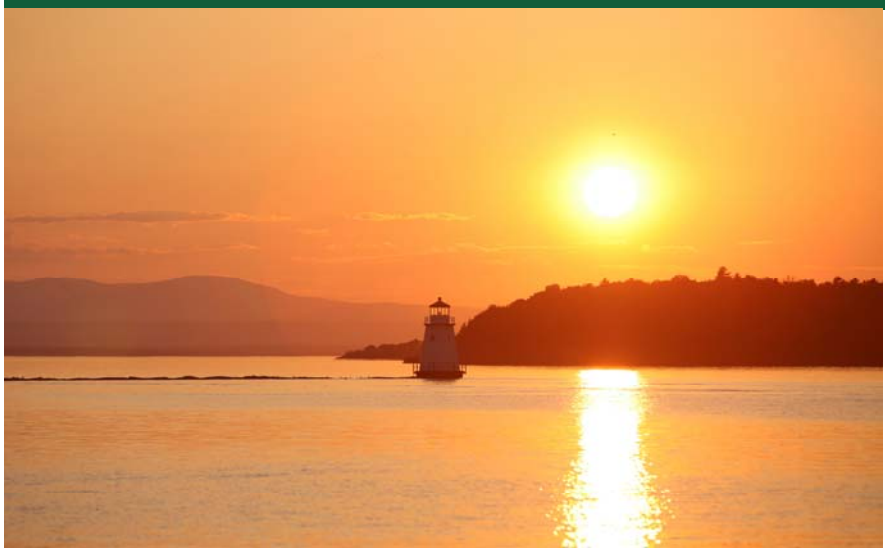
JULY, 2016

THE University of Vermont MEDICAL CENTER

Pathology & Laboratory Medicine

Communiqué

IN THIS ISSUE



Summer Holiday

Laboratory Service Center Hours

Lab Collection Site	Independence Day Monday, July 4, 2016	Labor Day Monday, September 5, 2016
Main Campus	Closed	Closed
Fanny Allen MOB	Closed	Closed
One South Prospect	Closed	Closed
Blair Park	Closed	Closed

Regularly scheduled hours will apply to any days not specifically addressed above. To view our regularly scheduled hours please go to UVMHealth.org/MedCenterDrawSites or call Laboratory Customer Service at 847-5121 or 1-800-991-2799.

LABORATORY TEST CATALOG

To view a complete listing of tests available at the University of Vermont Medical Center, please visit **http://uvmlabs.testcatalog.org**

Browse by Name

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Blood Bank Updates

UNIVERSAL IRRADIATION OF PLATELETS

The Blood Bank began irradiating all platelet components at the time of receipt on **April 18, 2016.** There will be no change in the way platelets are ordered for transfusion. Please continue to indicate the clinical need for irradiation on transfusion orders because red blood cell products are NOT impacted by this change. Irradiation for red blood cell products will be performed at the time of issue for transfusion. Universal irradiation of platelet products was approved by the UVM Medical Center Transfusion Committee.

ELIMINATION OF CMV NEGATIVE BLOOD PRODUCTS

The Blood Bank began phasing out the use of CMV seronegative blood products on **May 1, 2016**. Only CMV reduced-risk (i.e. leukoreduced) blood products will be provided to patients at UVM Medical Center. The exception will be for intrauterine transfusions, where the Blood Bank will provide CMV seronegative and CMV reduced-risk red blood cells. Elimination of CMV seronegative blood products was approved by the UVM Medical Center Transfusion Committee and is in alignment with standard of care across many academic hospital transfusion services in the US, Canada, and Europe.

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Chemistry Updates

METHOTREXATE TESTING CHANGE IN METHODOLOGY

On June 27, 2016 the Chemistry Laboratory changed the instrument used for measuring methotrexate levels from the TDX/FLX (Abbott Laboratories, Abbott Park, IL) to the Vitros 5600 (Ortho Clinical Diagnostics, Raritan, NJ) using reagents from Ark Diagnostics (Fremont, CA). This change is taking place because Abbott Laboratories is discontinuing support for the TDX/FLX; an instrument that in various forms has been used in the laboratory for over 25 years. Both instruments utilize immunoassays and correlations between the methods look very good.

It should be noted that no immunoassay should be used to measure methotrexate levels in patients who have received carboxypeptidase G2 (Glucarpidase) as a high dose methotrexate rescue therapy, until at least 48 hours after the dose is given. These patients have increased levels of DAMPA, a metabolite of the enzyme action on methotrexate, that cross reacts with the antibody used in these assays. An LC-MS/MS methodology is available from Mayo Medical Laboratories for use in these circumstances, although there would be a delay in the availability of these results.

Additional Test Codes					
Primary ID	**SQ Code**	**PRISM Code**	**Mayo Access ID**		
MTXT	MTXT	LAB2561	FAH5718		
Specimen Information					
Container	Specimen	Temp.	Collect	Submit	Minimum
Red Top Tube, Plain	Serum	Refrigerate	4 mL	1 mL	0.5 mL
Sample MUST be protected from light; wrap tube in foil. Serum gel tube is NOT acceptable.					
Test Schedule	**Reference Range**	**CPT**			
Daily / 24 Hours / Available STAT	Therapy Dependent	Methotrexate Quant: 80299			

HEPATITIS C INFECTION TEST CHANGES

The CDC issued a guideline in 2012 recognizing the ineffectiveness of the then current risk based strategy for Hepatitis C screening and recommended screening of all persons born between 1945 and 1965 for chronic hepatitis C infection. Recent advances in therapy for this disease have emphasized the importance of recognizing and treating this disease. As part of the CDC recommendation, it was stated that HCV RNA test should be performed on patients who have tested positive for antibody to hepatitis C and that this result should be used to identify those with an active HCV infection.

On May 25, 2016 the Chemistry Laboratory began offering Hepatitis C Antibody with Reflex to HCV RNA PCR as a screening test for Hepatitis C. A Positive hepatitis C antibody will include a reflex test so that all low level reactive or reactive antibody tests will be followed with an HCV RNA (PCR) Quantitative test at an additional charge. The minimum sample volume for this test is 1.2 mL of serum, an increased sample volume is needed to support reflex testing. This test should not be ordered on patients who have previously tested positive for hepatitis C antibody.

Additional Test Codes

Primary ID	SQ Code	PRISM Code	Mayo Access ID
HCSCR	HCSCR	LAB3348	N/A

Reflex Criteria for Hepatitis C Antibody W/ Reflex PCR

Initial Test	Reflex Criteria	Reflex Test	CPT
Hepatitis C Antibody	Low Level Reactive or Reactive	HCV RNA (PCR) Quantitative	87522

You have the option to decline reflex testing if you believe it is not medically necessary.

Sample Requirements

Container	Specimen	Temperature	Collect Vol	Submit Vol	Minimum Vol
SST	Serum	Frozen	8 mL	2.0 mL	**1.2 mL**
Serum must be separate from cells within 24-hours of collection. Stable 3 days refrigerated and 6-weeks frozen.					

If the patient has previously been positive for hepatitis C antibody, **the test will not be performed** but the HCV RNA by PCR will be performed and reported.

The Hepatitis C RNA (PCR) Quantitative will continue to be available as a separately orderable test for monitoring therapy (Test Code: HCVQU, PRISM Code LAB2472).

The Hepatitis C Antibody test will be inactivated as a stand alone test.

Reference

Centers for Disease Control and Prevention. Recommendations for the identification of chronic hepatitis C virus infection among persons born during 1945-1965. MMWR 2012;61(RR-4):1-32

SYRINGE DISPOSAL

The University of Vermont Medical Center does not accept sharps for disposal from patients!
Chittenden Solid Waste District (CSWD) will accept needles that are packaged according to the instructions outlined in their pamphlet “GET THE POINT: Be safe with syringes and other sharps”. CSWD also has bright orange stickers to attach to a syringe container to warn handlers to be careful. These items are available at any CSWD location. You can also order them so that they are available for patients at your office 872-8111 or visit www.cswd.net

Chemistry Updates continued

HELICOBACTER PYLORI STOOL ANTIGEN TEST TO REPLACE THE HELICOBACTER PYLORI ANTIBODY SEROLOGY TEST

On May 27, 2016 the Immunology Laboratory began offering the Meridian Bioscience (Cincinnati, OH) Premier Platinum HpSA PLUS *Helicobacter pylori* Stool Antigen Test and discontinued offering the *H. pylori* Antibody serology test (HPYS). A recent Communiqué from Mayo Medical Laboratories (January/February 2016: Communiqué - Helicobacter pylori Infection: Serologic Testing Not Recommended - Mayo Medical Laboratories) discusses how serologic testing was omitted as an acceptable diagnostic method for the diagnosis of functional dyspepsia in a recent New England Journal of Medicine review article. In addition, established guidelines from both the American Gastroenterology Association (AGA) and the American College of Gastroenterologists (ACG) recommend either the urea breath test (UBT) or the *H. pylori* stool antigen test (SAT) as the preferred test methods for active *H. pylori* infection. Due to the persistent nature of antibodies to *H. pylori*, active disease requires confirmatory testing by an alternative assay such as the UBT or SAT. Finally, an increasing number of health insurance providers, including Aetna, Geisinger Health Plan, and Cigna, are no longer reimbursing patients for *H. pylori* serologic testing.

The Premier Platinum HpSA PLUS enzyme immunoassay is a qualitative test for the detection of *Helicobacter pylori* antigens in fecal specimens. The antigen is only present in active disease and the results can be used both to aid in the diagnosis of *H. pylori* infection and to monitor response during and post-therapy. This is an FDA approved test for both adult and pediatric patients. Antimicrobials, proton pump inhibitors and bismuth preparations are known to suppress *H. pylori* and ingestion of these prior to *H. pylori* testing (culture, histology, rapid urease, UBT, antigen) may give a false negative result.

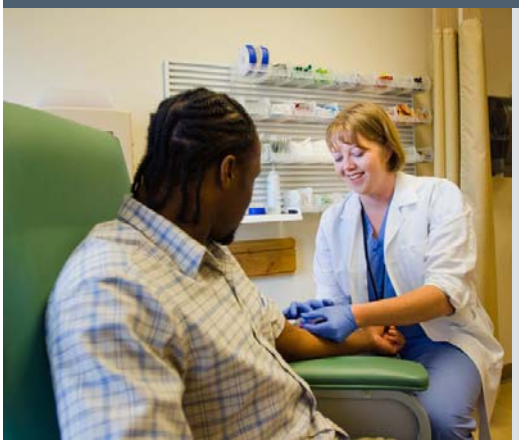
Helicobacter pylori is now recognized as one of the most common and medically important pathogens worldwide. *H. pylori* has been firmly established as an etiologic agent in chronic gastritis and peptic ulcer disease, and has been associated (rarely) with mucosa-associated lymphoid tissue (MALT) lymphoma and gastric adenocarcinoma. Therefore, the accurate diagnosis and prompt initiation of antibiotic therapy are important for successful disease resolution.

If you have any questions concerning this test update please contact the Immunology Laboratory at (802) 847-7638.

References:

1. Mayo Medical Laboratories Communiqué, January/February 2016, *Helicobacter pylori* Infection: Serologic Testing Not Recommended, Vol. 41, No. 1.
2. Premier Platinum HpSA PLUS Product Insert, Meridian Biosciences Inc., Cincinnati, OH.

LABORATORY PATIENT SERVICE CENTER



Main Campus
Main Pavilion, Level 2
111 Colchester Avenue
Burlington, VT

One South Prospect
1 South Prospect St
First Floor Lobby
Burlington, VT

Fanny Allen Campus
792 College Parkway
Colchester, VT

Adult Primary Care Williston
353 Blair Park Road
Williston, VT

Visit UVMHealth.org/MedCenterDrawSites for patient service center hours and special test considerations.

All UVM Medical Center phlebotomists are nationally certified

Helicobacter Pylori Stool Antigen Testing	
Test Name:	H. Pylori Antigen
SQ Code:	HPSA
PRISM Code:	LAB1016
CPT Code:	87338
LOINC Code:	17780-8
Division:	Immunology
Method:	Enzyme-Linked Immunosorbent Assay (ELISA)
Instrumentation:	Dynex DSX
Specimen Collection and Preparation:	5 g (walnut sized) fecal specimen collected into a sterile airtight container (without preservatives) and stored at 2-8 C until tested. The specimen may be held at 2-8 C for up to 72 hours prior to testing. If testing cannot be performed within this time frame or for shipment, specimens should be frozen immediately upon receipt and stored frozen (-20C to -80C) until tested. Stable frozen up to 60 days. Minimum volume is 100 uL of well-mixed liquid or semi-solid stool and 5-6 mm diameter of well-mixed formed/ solid stool.
Specimen Note:	Stool in transport media, swabs, or preservatives are unacceptable. Performance characteristics have not been established for watery, diarrheal stools. Stool must be mixed thoroughly.
Test Schedule/Analytical Time/Test Priority	Tuesday and Thursday / Same day / Not available STAT
Reference Range:	Negative
Interpretation:	Positive: Indicates the presence of *H. pylori* antigens. Negative: Indicates the absence of *H. pylori* antigens, or that the level of antigen is below the cut-off of the assay.
Limitations:	False negative results may be obtained within 2 weeks of treatment with antimicrobials, bismuth, or proton pump inhibitors. A negative result in such a situation should be followed up with repeat testing at least 2 weeks after discontinuation of therapy.
New York State Approved:	Yes
Effective Date:	May 27, 2016

Chemistry Updates Continued

IRON BINDING CAPACITY POSITIVE BIAS NOTED BETWEEN 4/25/2016 TO 5/30/2016

We have been notified by the manufacturer of the reagents used for total iron binding capacity on the Vitros 5600 (Ortho Clinical Diagnostics) in the Chemistry Laboratory that the reagents in use 4/25/2016 to 5/30/2016 contained Assay Data Diskettes with incorrect values that resulted in a positive bias in results. The degree of bias depended on the level of result, with higher results having a higher degree of bias.

The incorrect calibration values were corrected on 5/31/2016. Samples run before and after correction indicated that for samples run between 4/25/2016 and 5/30/2016 total iron binding capacity results were biased approximately:

3% high in the range 150 – 200 ug/dL

8% high in the range 200 – 300 ug/dL

11% high in the range 300 – 400 ug/dL

13% high in the range 400 – 500 ug/dL

We expect results in the reference range to be biased by approximately 10%. In the majority of cases this should not result in a clinically significant change in interpretation. If you have any questions concerning this notice, please contact Dr. Greg Sharp (gregory.sharp@uvmhealth.org) in the Chemistry Laboratory.

VISCOSITY TESTING TO BE SENT TO MAYO MEDICAL LABORATORIES

Beginning July 7, 2016 we will no longer perform viscosity testing at UVMMC. The methodology currently used at UVMMC has changed little from the original description of Waldenstrom's use of an Ostwald tube in 1944([2]). Viscosity is measured as the time required for a serum sample to flow through a restricted tube by gravity compared to water. The simplicity of this method, however, hides issues of standardization and precision expected of more current technologies.

The testing is important when patients with hypergammaglobulinemia or multiple myeloma develop a hyperviscosity syndrome characterized by oronasal bleeding, neurologic symptoms, blurred vision, and heart failure. Viscosity depends on both the amount and properties of the paraprotein. For patients with an IgG paraprotein as in multiple myeloma, the increase in viscosity is roughly proportional to the concentration of the paraprotein, whereas for IgM paraproteins, relative viscosity can rise exponentially above a concentration of 3 g/dL([1]). Therapy is directed at symptomatology, although the level at which symptoms occur seems to be consistent within individual patients.

We will send Viscosity testing to our reference lab partner Mayo Medical Laboratories (MML). Their laboratory uses an instrument which measures the power required to oscillate a probe at a constant rate in the serum sample. The increased power required in sera with increased viscosity is calibrated by standards of known viscosity. This analysis is automated and requires much less sample (1.5 mL). Unlike the current UVMMC methodology which reports results as a ratio, these results are reported in units of viscosity, the poise. Since water has an approximate viscosity of 1 centipoise (cP), units reported by the Ostwald tube (used at UVMMC) are roughly comparable to those of the system used at MML. Viscosities greater than 1.5 cP are considered abnormal: however, hyperviscosity is rarely present unless the viscosity is greater than 3.0 cP by the MML system. This methodology is used currently for samples for which an adequate volume is not available. The change to Mayo Medical Laboratories will take place on July 7, 2016. If you have any questions concerning this change please contact Dr. Greg Sharp (gregory.sharp@uvmhealth.org) in the Chemistry Laboratory.

References

1. Fahey JL, Barth WF, Solomon A. Serum hyperviscosity syndrome. JAMA 1965;192(6): 120-123.
2. WaldenstromJ. Incipient myelomatosis or essential hypergammaglobulinewia with fibrinogenopenia: a new syndrome? Acta Med Scand. 1944;117: 217-247.

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Coagulation Laboratory Update

WARNING: AGE ADJUSTED D-DIMER CUTOFF VALUES

The recent Best Practice Advice from the American College of Physicians (ACP) recommends age adjusted D-dimer cutoffs for investigating a VTE stating in patients over 50 years of age:

"Best Practice Advice 4: Clinicians should use age-adjusted d-dimer thresholds (age × 10 ng/mL rather than a generic 500 ng/mL) in patients older than 50 years to determine whether imaging is warranted [(1)]."

However, this recommendation has created potential patient safety issues. At this time, we do not recommend using age-adjusted d-dimer cutoff thresholds with our D-dimer assay at UVM Medical Center.

D-dimer Assay at UVMMC Laboratories

1. The Thrombosis and Hemostasis Laboratory at the University of Vermont Medical Center utilizes a D-dimer assay which is only validated for a VTE cutoff value of 230 D-DU ng/mL; D-DU corresponds to a D-dimer Unit.
2. Any use of the age-adjusted cutoff value is a post-analytic modification of this FDA-approved test and is considered "off-label" use of the test result. Our laboratory does not have literature to support the validity of age-adjusted cutoff for our specific assay.

Because D-dimer rises with age, it is less useful to exclude venous thromboembolism (VTE) in patients over 50 years of age. The major article by Marc Righini et al. used to support the Best Practice Advisor failed to report the unit type with their D-dimer cutoff (2). From the D-dimer assays used in the article, one can deduce that "500 ng/mL" refers to 500 FEU ng/mL.; FEU corresponds to a **F**ibrinogen **E**quivalent **U**nit. The UVMMC laboratory reports the D-dimer as a **D**-**d**imer **U**nit.

Additionally, the FDA requires a manufacturer of a D-dimer assay to perform a clinical management study for exclusion of VTE using the assay specific cutoff. In the manuscript by Righini el al., the age-adjusted cutoff for the D-dimer assays was not investigated individually for each assay; instead, the results of 6 different D-dimer assays were evaluated as a group in the study [(2).]

References

1. Raja AS, Greenberg JO, Qaseem A, et al. Evaluation of patients with suspected acute pulmonary embolism: best practice advice from the clinical guidelines committee of the American College of Physicians. Ann Intern Med 2015;163:701-711.
2. Righini M, Van Es J, Den Exter PL, Roy PM, Verschuren F, Ghuysen A, et al. Age-adjusted D -dimer cutoff levels to rule out pulmonary embolism: the ADJUST-PE study. JAMA 2014;311:1117-24.

NEW TESTING ALGORITHM: LUPUS ANTICOAGULANT CASCADE

The Thrombosis and Hemostasis Laboratory is pleased to offer a Lupus Anticoagulant Cascade to aid in the diagnosis of anti-phospholipid antibody syndrome associated with thrombosis. This assay went live June 15, 2016, and **the Silica Clotting Time and Dilute Viper Venom will no longer be orderable as stand alone tests.**

(Continued on page 8)

Anti-phospholipid syndrome (APS), the most common cause of acquired thrombophilia, is associated with significant morbidity and mortality across diverse patient populations. The most frequently detected antibodies are commonly referred to as lupus anticoagulants (LA) due to their prevalence in patients with systemic lupus erythematosus. However, the antibodies, known as anti-phospholipid antibodies (APA) associated with APS are extremely heterogeneous and are directed against a wide variety of anionic phospholipids, including cardiolipin, ß2 glycoprotein 1 (B2GP1), cell-membrane phosphatidylserine, and many others. While these antibodies most commonly cause *in vivo* thrombosis, these same antibodies paradoxically prolong *in vitro* clot-based laboratory assays. A panel of tests is necessary to detect APAs as no single test presently available is sufficient to detect (or exclude) this diverse group of antibodies. The LA Cascade is provided (see below) as an overview of the recommended laboratory testing and should not supplant the diagnostic interpretation provided by the Thrombosis and Hemostasis Laboratory.

LUPUS ANTICOAGULANT (LA) TESTING

Based upon consensus criteria from the International Society for Thrombosis and Hemostasis (ISTH), confirmation of a LA requires that the following criteria are met:

- Performing 2 or more phospholipid-dependent clotting tests demonstrating prolongation of at least one test (i.e. Silica Clot Time (SCT), dilute Russell Viper Venom Test (dRVVT))
- Evidence for inhibitory activity shown by the effect of patient plasma on normal pooled plasma. (i.e. mixing study which fails to show complete correction)
- Demonstration of phospholipid-dependence of the inhibitor on a confirmatory test as evidenced by shortening of the clotting time with the addition of additional phospholipid.

Equally important, the ISTH recommends the following are performed:

- Routine clotting tests such as the prothrombin time (PT) and partial thromboplastin time (aPTT) to evaluate for the possibility of other coagulation disorders, particularly those which interfere with LA testing methods
- Factor assays whenever there is a suspicion of a specific factor deficiency or inhibitor

The laboratory criteria include positive testing for one of the following on 2 or more occasions, at least 12 weeks apart:

1. Lupus anticoagulant
2. Cardiolipin antibodies (IgG or IgM) in medium or high titer, and/or
3. b2-glycoprotein 1 antibodies (IgG or IgM)

Though rare, a factor-specific antibody to factor VIII can result in false positive LA testing; as part of the diagnostic interpretation, the laboratory will ask the ordering medical provider to exclude the likelihood of a factor specific inhibitor. Factor activity assays can be performed upon request.

INTERPRETATION OF LABORATORY TEST RESULTS

The Clinical Laboratory Standards Institute (CLSI) published updated 2014 guidelines for the laboratory diagnosis of APA. These guidelines state that all laboratory results and calculations in the laboratory's LA panel must undergo a step-by-step review by a qualified individual knowledgeable of the specific assays, and a written summary interpretive report must be provided to the ordering physician(s). The Thrombosis and Hemostasis Laboratory will provide a written interpretation for all LA Cascade testing.

The diagnosis of APS requires both clinical and laboratory pathologic evaluations. In addition to clinical criteria, often presenting as vascular thrombosis or pregnancy morbidity, persistently positive laboratory tests are required to render a diagnosis of APA because of transient low level increase of APA in many clinical conditions including infections and reactive processes. **Testing during the acute phase (i.e. at the initial presentation of thrombosis) is not recommended.** Consensus guidelines suggest testing should ideally occur when the patient is not taking anti-coagulation medications.

CARDIOLIPIN AND B2-GLYCOPROTEIN 1 ANTIBODIES (IGG AND IGM)

Please note, the solid phase testing necessary to detect cardiolipin or b2-glycoprotein 1 antibodies are not included in this LA Cascade laboratory testing panel, and these assays must be ordered independently by the medical provider (Order codes CARDLI and B2PNL, respectively). These solid phase tests require serum samples and cannot be "added on" to the plasma samples used for the Lupus Cascade. Should the results from these solid phase assays be available at the time of the LA Cascade, the Thrombosis and Hemostasis Laboratory will incorporate these results into the final diagnostic interpretation.

ROUTINE COAGULATION SCREENING ASSAYS

The prothrombin time (PT) and activated partial thromboplastin time (aPTT) time are not included in this Lupus Anticoagulant Cascade. Medical providers must consider ordering these screening assays as part of their diagnostic work-up to further evaluate the possibility of other coagulation disorders.

DIRECT ORAL ANTI-COAGULANTS (DOAC)

Consensus guidelines suggest testing should only occur when the patient is free from oral anticoagulation medications including warfarin and the Direct Oral Anti-Coagulants (DOAC) medications such as dabigatran, rivaroxaban, apixaban, and edoxaban.

EXISTING LUPUS ANTICOAGULANT AND ANTI-PHOSPHOLIPID PANELS ARE DISCONTINUED

With this new Lupus Cascade, the previous panels will be discontinued:

1. Order Code APAB: DRVVT, aPTT 50:50 mix, and cardiolipin antibodies
2. Order Code LAW: DRVVT and aPTT 50:50 mix

The aPTT available at the UVMMC Laboratories is only rated moderately sensitive to the presence of a lupus anticoagulant based on the phospholipid content in the reagent system. One must consider this fact if the aPTT is utilized as a screen for a lupus anticoagulant. The new Lupus Cascade utilizes the Dilute Russell Viper Venom Test and the Silica Clot Time, both of which have increased sensitivity for detecting a lupus anticoagulant when compared to the current aPTT assay. Additionally, the Lupus Cascade will automatically perform both these tests fulfilling the recommended ISTH and CLSI guidelines of utilizing 2 phospholipid-dependent clotting assay systems.

Continued on page 10

LA Cascade Test Information	
Test Codes	SQ Code: LACASC | PRISM Code: LAB3629 | Mayo Access ID: FAH5675
CPT	DVV-85613, SCT-85732, Interpretation-85390-26, THT-85670 (if appropriate), FIB-85384 (if appropriate), ANTXAQ-85520 (qualitative anti-Xa, if appropriate), HEPAS- 85525 (if appropriate)
Price:	Please contact Laboratory Customer Service for pricing information
Division:	Coagulation
Sample Requirements	Collect 14 mL blue top tube (4 tubes) submit 4 mL Plasma Frozen. After collection samples must be kept at ambient temperature until they are processed. Samples must be processed within 3 hours of collection. If the samples cannot be processed within 3 hours call Laboratory Customer Service for a courier pickup or have the sample collected at the Main Campus. **Submit four separate frozen plasma aliquots of 1mL each for this testing. *Refer to Coagulation Specimen Handling for process instructions prior to collection. Submit separate frozen plasma aliquot for this test. Draw blood in light blue top tube(s). Spin down, remove plasma, spin plasma again and place citrate platelet-poor plasma in required number of plastic vials (Glass vials cannot be accepted.) Freeze specimen at ≤-30° C if possible. Send specimen frozen on dry ice. Each coagulation assay requested should have its own vial.
Expected Value	Lupus anticoagulant not detected
Test Schedule	Tuesday and Thursday/Reported next day/Not available STAT
Instrumentation:	ACL TOP 500
NYS Certified:	Yes
Effective Date	June, 16 2016

Order Code	Test ID	Test Name	Available Separately	Always Performed
LACASC	DVV	Dilute Russell Viper Venom Time (DRVVT), Screen	No	Yes
	LLAC	Dilute Russell Viper Venom Time (DRVVT), Confirm	No	No
	SCT	Silica Clot Time (SCT), Screen	No	Yes
	SCTC	Silica Clot Time (SCT) , Confirm	No	No
	LACINT	Interpretation	No	Yes
	DVV50	DRVVT Mixing Study	No	No
	SCT50	SCT Mixing Study	No	No
	THT	Thrombin Time (TT)	Yes	No
	THTHEP	TT, hepzyme	No	No
	ANTXAQ	Anti-Xa, qualitative	No	No
	SCTHEP	SCT, hepzyme	No	No
	DVVHEP	DRVVT, hepzyme	No	No
	FIB	Fibrinogen	Yes	No

REFERENCES:

- Keeling D., et al. Guidelines on the investigation and management of antiphospholipid syndrome. BJH. April, 2014; 157(1): 47–58.
- Ledford-Kraemer M., et al. H60-A: Laboratory Testing for the Lupus Anticoagulant; Approved Guideline. Clinical and Laboratory Standards Institute. April, 2014; 34(6): 1-93.
- Levin JS, Branch DW, Rauch J. The antiphospholipid syndrome. New Engl J Med. March 7 2002; 346(10): 752-763.
- Moore GW. Recent Guidelines and Recommendations for Laboratory Detection of Lupus Anticoagulants. Semin Thromb Hemost 2014; 40: 163–171.
- Pengo V., et al. Subcommittee on Lupus Anticoagulant/Antiphospholipid Antibody of the Scientific and Standardisation Committee of the International Society on Thrombosis and Haemostasis. Update of the guidelines for lupus anticoagulant detection. J Thromb Haemost 2009; 7(10): 1737–1740.

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Microbiology Updates

URINE FUNGAL CULTURE: NEW TEST APPROVAL POLICY

On June 27, 2016 the Microbiology Laboratory began to result urine fungal culture results with the following statement:

"Bacterial culture, Urine is the appropriate order for the detection of Candida spp. Fungal culture of urine should only be performed to diagnose invasive fungi (Cryptococcus, Aspergillus, Mucormyctes, Blastomyces and Histoplasmosis".

If you suspect an invasive fungi urinary tract infection, please contact the Microbiology lab for pathology approval (802-847-2339).

Additional Test Codes

Test Name	Test Code	PRISM Code	Mayo Access ID
Fungus Culture, Other	FC	LAB240	FAH5074
Fungus Culture, Other & Smear	FCS	LAB242	FAH5076

INFLUENZA A SUBTYPING NO LONGER OFFERS

Effective 6/27/16 Microbiology will no longer offer Influenza A subtyping on Respiratory samples (Order code **RESVD**) that are Influenza A positive. For up-to-date influenza epidemiologic data, please visit the Vermont Department of Health website:

http://healthvermont.gov/prevent/flu/flusurveillance.aspx

NEW MICROBIOLOGY COLLECTION KITS WITH IMPROVED FLOCKED SWAB

UVMMC is introducing a new swab for use as a collection device for Microbiology testing. Flocked swabs (FloqSwab) have been shown to improve the quality of sample collection. In contrast to other cotton swabs which entrap sample material, the specimen stays close to the surface of the flocked swab and is released into the liquid media which is then used for testing.

NEW BACTERIAL, FUNGAL (YEAST) COLLECTION KIT
AND
NEW VIRAL COLLECTION KIT

See page 16 for information..

Myositis Panel II – Antibody testing

A diagnosis of myositis is usually made from a combination of clinical exam, electro-diagnostic testing, biopsy and blood work. Many patients are now also tested for myositis specific antibodies. These antibodies can aid in the differential diagnosis of inflammatory myopathies and provide a confirmatory diagnosis and prognostic information. About 50% of patients with polymyositis or dematomyositis have myositis specific antibodies.

There are dozens of myositis-specific and myositis associated antibodies however there are a handful for which we have significant information on how these serological subtypes behave clinically and prognostically.

Currently there are several myositis panels which generally overlap in the most common myositis-specific and myositis associated antibodies. Our institution will default to the myositis II panel which includes the most common autoantibodies including anti jo-1. Because of the overlap myositis panel I and jo-1 will not be available to order. The tests remain available just bundled as one order (myositis II panel) which is more efficient and cost effective.

TEST CODE INFORMATION

PRISM Order Code: LAB2715 | SQ Order Code: MYOABP | Mayo Access ID: FMYOP

A brief review of the antibodies tested and their utility is as shown below.

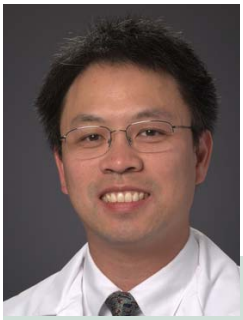
MYOSITIS SPECIFIC ANTIBODIES:

Anti –aminoacyl -tRNA synthetase (ARS) antibodies include:

- **Jo-1 antibody** – PL-7, PL-12, EJ, OJ; Jo -1 is the most common of these. These antibodies are associated with the anti-synthetase syndrome which includes ILD, myositis, arthritis, Fevers and Raynaud's.
- **Anti - SRP** -Generally these patient have severe muscle weakness of rapid onset, myalgia's and cardiac involvement. Generally these patients have aggressive disease and are difficult to treat.
- **Mi-2** -Myositis-specific antibody; may have the classic dermatomyositis skin changes.

MYOSITIS ASSOCIATED ANTIBODIES: OFTEN FOUND IN MYOSITIS AS PART OF OVERLAP SYNDROMES

- **Anti-Ku**
- **P155/140-** Myositis-specific antibody: most commonly found in children with juvenile dermatomyositis. In adults it is also associated with Cancer associated dermatomyositis. These antibodies are not associated with ILD.
- **Anti-PM/ Scl Ab-**Associated with ILD/pulmonary fibrosis and is an overlap of polymyositis and scleroderma.
- **U2SNRP**



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HLA Updates

HLA CROSSMATCH TUBE CHANGE

On July 11, 2016 the HLA Laboratory will change its preferred tube type for crossmatches from Special Heparin to ACD tubes. ACD tubes are recommended by the American Society of Histocompatibility and Immunogenetics, and several studies cite extended T and B cell viability over heparin tubes. These tubes are commercially available and do not need to be refrigerated.

Starting July 11, 2016, please discard any remaining Special Heparin Tubes and replace them with ACD tubes. See “Special Heparin Tubes Discontinued” for ordering instructions for ACD tubes below.

SPECIAL HEPARIN TUBES DISCONTINUED

UVM Medical Center Laboratory will no longer provide Special Heparin tubes for any testing. All testing that previously required this in-house prepared tube has changed its preferred tube type. Please refer to the Joint Test Catalog (JTC) or below for the preferred tube type.

NOTE: **Not all tests have changed to the same tube type.**

Ordering replacement tubes.

Flow Cytometry – Na Heparin (green top)

Cytogenetics – media tube or Na Heparin (green top)

HLA/Tissue Typing – ACD (yellow top)

NEW CELIAC DISEASE PANEL

On June 24, 2016, the HLA Laboratory began offering a Celiac-Associated HLA DQ Alpha and DQ Beta testing. HLA currently offers HLA DQ Alpha 1 and DQ Beta 1 testing and now the ordering of these tests for Celiac Disease Association will be easier. Previously when testing for celiac HLA DQA1 and DQB1, a generic HLA DQ test was ordered and a comment was placed by the ordering provider if the testing was for celiac disease. Now a provider can order a single test, CELIDQ to receive the HLA DQA1 and DQB1 typing and an interpretive assessment.

Clinical Application

Celiac Disease (gluten-sensitive enteropathy) is mediated by T lymphocytes in patients with genetic susceptibility. This genetic association is with certain HLA genes in the class II region (HLA DQ alpha 1, DQ beta 1).

HLA DQA1 and DQB1 typing are useful for assessing the risk of celiac disease.

The UVM Medical Center results for this test will include the HLA DQA1 and DQB1 typing and an interpretive risk assessment.

Method

Testing is performed by Polymerase Chain Reaction/Reverse Sequence Specific Oligonucleotide Probe (PCR/rSSOP) at a low to intermediate resolution which uses sequence-specific oligonucleotide probes (SSO) bound to fluorescent coded microspheres (beads) to identify alleles encoded by sample DNA. DNA typing is analyzed by Luminex technology.

The assignment of the HLA typing is based on the reaction pattern compared to patterns associated with published HLA gene sequences and can discriminate a single nucleotide change.

Continued on page 11

New Celiac Disease Panel Continued from page 13

Limitations

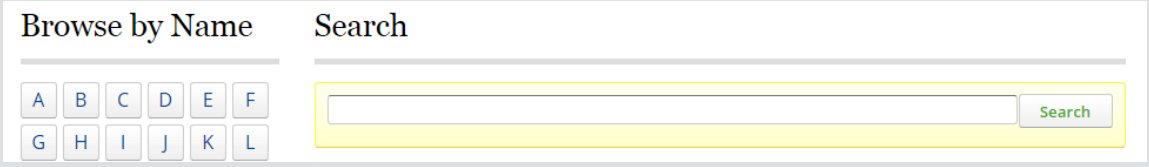
It is important to realize that these genes are also present in about approximately 20% of the population without celiac disease. Therefore, the presence of these genes does not prove the presence of celiac disease or that genetic susceptibility to celiac disease is present.

Specimen Information

Important note			
HLA typing samples should not be shared. This test should have a separate sample tube.			
Additional Test Codes			
Primary ID	**SQ Code**	**PRISM Code**	**Mayo Access ID**
CELIDQ	CELIDQ	LAB3581	FAH5719
Celiac Disease Panel Specimen Information			
Container	**Specimen**	**Temp.**	
Lavender Top Tube	Whole Blood	Refrigerate	
Collect Volume	**Submit Volume**	**Minimum Volume**	
2.5 mL	2.5 mL	1.5 mL	
Tube SHOULD be full, do not spin. Specimen must be labeled with collection date and at least 2 patient identifiers. Specimen is stable at room temperature for 24 hours and at 2-8°C for 30 days, consult HLA department for other situations.			
Test Schedule			
Monday - Friday / 5 days / Not available STAT			
CPT			
81376 x 2			
New York State Approved			
Yes			
Effective Date			
June 24, 2016			

LBORATORY TEST CATALOG

To view a complete listing of tests available at the University of Vermont Medical Center, please visit **UVMLabs.TestCatalog.org.**



New Sample Collection Supplies

BLOOD CULTURE VIAL CHANGE

The Laboratory will be transitioning to new blood culture vials some time in August 2016.
The new vials are shatterproof plastic. Old bottles will be acceptable as long as they have not expired.. There are no changes in volume or collection procedures.

New Adult Blood Culture Vials

Old Adult Blood Culture Vials

New Pediatric Blood Culture Vial

Old Pediatric Blood Culture Vial

NEW FORMALIN VIALS

In an attempt to make sample vials containing formalin more recognizable, the Department of Pathology has worked with our vendor to change the labeling from white to a bright green.

Pathology and Purchasing will be working to cycle out all of the older (white label) containers. If you have any white labeled stock in your inventory, please return it to the following address:

UVMMC Department of Pathology

ATTN: Formalin container replacement

NEW MICROBIOLOGY COLLECTION TUBES

UVMMC is introducing a new swab for use as a collection device for Microbiology testing. Flocked swabs (FloqSwab)have been shown to improve the quality of sample collection. In contrast to other cotton swabs which entrap sample material, the specimen stays close to the surface of the flocked swab and is released into the liquid media which is then used for testing.

The new collection devices will be available June 15, 2016. During the transition phase, **swabs currently in use will be accepted.**

NEW BACTERIAL, FUNGAL (YEAST) COLLECTION KIT

White cap tube w/ liquid Amies media and a regular ESwab (included)

USE FOR: Wounds, MRSA PCR, Group B strep PCR, throat Strep screen, Fungal (yeast), vaginitis exam and *Trichomonas* antigen

NEW VIRAL COLLECTION KIT

Red Cap M6 media with a Flexible FloqSwab (included)

USE FOR: Viral Molecular (PCR) detection

PLEASE NOTE THE EXPIRATION DATE ON THE COLLECTION VIALS AND SWABS PRIOR TO USE.

Collection kits are stored at room temperature, after inoculation vials are stored refrigerated.

WOODEN SWABS ARE NOT ACCEPTABLE:

Chemicals used during manufacturing of wooden swabs may be toxic to infectious agents. Do not use wooden swabs for collection of samples for Microbiology..

Spotlight on the Lab

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LABORATORY OUTREACH

It may surprise some of you to know that the hospital laboratory here at UVM Medical Center also serves as a reference lab for almost all of the private practice clinicians in Chittenden County, our UVM Health Network partners, the other hospitals in Vermont, upstate New York and even a few hospitals in New Hampshire.

Laboratory Outreach allows us to reach beyond our own hospital inpatient and outpatient population to serve the needs of patients and clinicians in our community. It has enormous healthcare benefits for any laboratory with the resources to provide an outreach program.

First and foremost it allows us to provide an **integrated inpatient and outpatient record** for people living here in Chittenden County. As we return the patient results to the physician's office for treatment and monitoring of their health, we also record and track the test results in our Prism medical record system. That way if a patient is admitted or comes to the emergency department, they can be treated with a more complete picture of their current medical history and we don't need to repeat testing.

Most private practice offices now have their own electronic medical record (EMR), and they need to view patient results in their own practice chart. To meet that need we provide **interfaced orders and results** to those practices. Part of what outreach does is to facilitate the design and implementation of the interfaces with the EMR vendor in the practice.

The outreach business here at UVM constitute around 30% of our testing volumes. Not only does this volume allow us to utilize some of the additional capacity in our lab it allows us to **offer testing on a more frequent basis.** It also allows us to **offer low volume testing here in house** instead of having to send it out to a lab that would perform more specialized tests. This makes a big difference in turnaround time for patients and clinicians, reducing length of stay and allowing patients to be diagnosed and treated in a more timely fashion.

Additionally, the outreach volumes allow us to control costs per unit of service by negotiating volume discounts with suppliers and offer testing at a more reasonable cost than our volumes alone would warrant.

As a reference lab we are very cognizant of the service levels we offer to our clients as a way of distinguishing ourselves from our competitors. We are not large enough to offer the lowest prices, and we are determined to maintain the highest quality for our patients and clinicians, so we believe that listening to our clients to determine what service factors are most important to them makes their workflow easier and ultimately benefits patients.

As part of being a reference laboratory for the "non patient" population we encourage our clients to order supplies from us to ensure continuity with tubes, reagents and collection devices. These must be easy to use and be available quickly and easily to prevent large quantities of inventory at every site that eat up resources, and could outdate.

We deliver supplies and collect samples through an extensive courier network. We pick up at several of our hospital clients twice a day and at some doctors' offices even three times a day. These frequent pickups not only allow us to return results before the end of the work day to ensure effective clinical management but also allow us to unpack in smaller batches and provide faster turnarounds and fewer specimens rejected for integrity issues.

Together with Mayo Medical Laboratory, we offer educational opportunities to our clients on laboratory testing in general, new tests, trends in testing, and utilization management. We even offer customer service and phlebotomy training.

Ultimately our Outreach business benefits the lab, our clients and most importantly our patients.

Compliance Updates

MEDICARE PREVENTIVE SERVICE

Chlamydia/ GC Screening Coverage:

- Screening for chlamydial infection for all sexually active non-pregnant young women aged 24 and younger and for older non-pregnant women who are at increased risk
- Screening for chlamydial infection for all pregnant women aged 24 and younger and for older pregnant women who are at increased risk
- Screening for gonorrhea infection in all sexually active women, including those who are pregnant, if they are at increased risk

Frequency of Screening for chlamydia and gonorrhea:

- Pregnant women who are 24 years old or younger when the diagnosis of pregnancy is known, and then repeat screening during the third trimester if high-risk sexual behavior has occurred since the initial screening test.
- Pregnant women who are at increased risk for STIs when the diagnosis of pregnancy is known, and then repeat screening during the third trimester if high-risk sexual behavior has occurred since the initial screening test.
- Women at increased risk for STIs annually.

The high/increased risk individual sexual behaviors, based on the USPSTF guidelines, include the following:

- Multiple sex partners
- Using barrier protection inconsistently
- Having sex under the influence of alcohol or drugs
- Having sex in exchange for money or drugs
- Age (24 years of age or younger and sexually active for women for chlamydia and gonorrhea)
- Having an STI within the past year
- IV drug use (for hepatitis B only)
- In addition for men – men having sex with men (MSM) and engaged in high risk sexual behavior, but no regard to age

Coding for Chlamydia/GC per Medicare:

For screening for chlamydia, gonorrhea in women at increased risk who are not pregnant use the following diagnosis codes:

Z11.8 Encounter for screening for Chlamydia

Z11.3 - Encounter for screening for infections with a predominantly sexual mode of transmission

AND any of:

o Z72.89 - Other problems related to lifestyle

o Z72.51 - High risk heterosexual behavior

o Z72.52 - High risk homosexual behavior or

o Z72.53 - High risk bisexual behavior. (These diagnosis codes are used to indicate high/increased risk for STIs)

NOTE: Additional Diagnosis codes are needed for screening of pregnant women

Link to policy: https://www.cms.gov/site-search/search-results.html?q=ncd%20210.10

DRUG SCREENING FOR MEDICAID PATIENTS

Medicaid has a limit of 8 drug screening tests per month. **Prior Authorization is needed if more than 8 drug screening tests are requested.** When placing your order, please keep in mind that counselors also order drug screening tests therefore care of the patient should be coordinated to determine if the 8 maximum orders will be exceeded and prior authorization should be requested.

FACTOR 5 LEIDEN AND PROTHROMBIN COAGULATION FACTOR 2

As of April 1, 2016, per **Medicare's** LCD policy for Molecular Pathology Procedures (L35000),

-**Prothrombin Coagulation Factor 2** (CPT: 81240) and - **Factor 5 Leiden** (CPT: 81241)

"are no longer considered to be clinically efficacious: therefore, testing is not medically necessary."

Medicare will no longer pay for this testing. An **ABN form for Medicare patients** will be **required** to bill the patient for this testing.

NEW LCD- HEAVY METALS

There is a new Local Coverage Determination policy for Heavy Metals that went into effect 6/6/16. The policy is broken down by each heavy metal. Covering Diagnoses are specific to the heavy metal being tested.

Link to the Heavy Metal Policy: -https://www.cms.gov/medicare-coverage-database/details/lcd-details.aspx?LCDId=35074&ContrId=312&ver=6&ContrVer=1&CntrctrSelected=312*1&Cntrctr=312&s=55&DocType=Active&bc=AAgAAAIAAAAAAA%3d%3d&

UROVYSION TESTING : BLUE CROSS BLUE SHIELD OF VERMONT NOTICE OF NON-COVERAGE

On May 20, 2016, we received notification from BCBS VT that effective with dates of service on or after August 1, 2016,

Urovysion for Bladder Cancer (FISH) testing (CPT 88120) will be considered *investigational* and no longer a covered service for their customers.

Per their provider manual www.bcbsvt.com/provider page 9 "Waivers":

- Clear communication between the provider and patient has occurred either face to face or over the phone. The patient must be told that the testing will not be covered by BCBSVT and that the patient will be held financially responsible. The complete cost of the test must be disclosed.
- An "Advance Notice of Potential Non-Coverage by a Commercial Insurer" ABN Form for the testing must be signed by the patient and scanned into their medical records. For pricing please contact Lab Customer Service (pricing is a required field on this form). The form must be **completely filled o**ut and **should state that BCBSVT considers this testing investigational.**
- Unless otherwise requested by the patient, the claim should still be submitted to BCBSVT so that the patient has a copy of the denial to submit to HSA or some other type of healthcare spending account.

UVMMC providers should use the "Advance Notice of Potential Non-Coverage by a Commercial Insurer" ABN form # 037111 which is available on our website or call Lab Customer Service to have a form faxed to you.

THE University of Vermont MEDICAL CENTER

111 Colchester Avenue
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PATHOLOGY & LABORATORY MEDICINE COMMUNIQUÉ — JULY, 2016

PATHOLOGY & LABORATORY MEDICINE COMMUNIQUÉ

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FAX LABORATORY CUSTOMER SERVICE

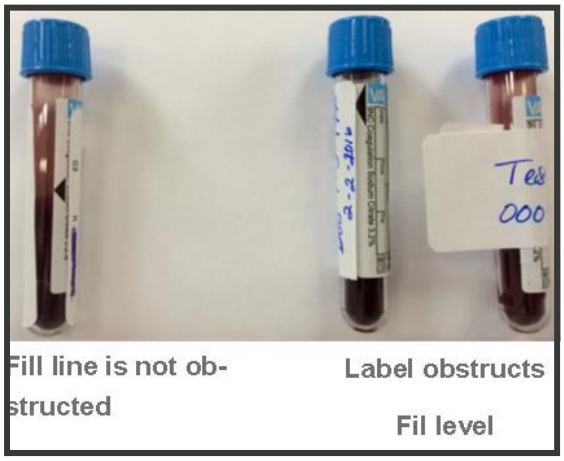
(802) 847-5905

WEBSITE

UVMLabs.TestCatalog.org/

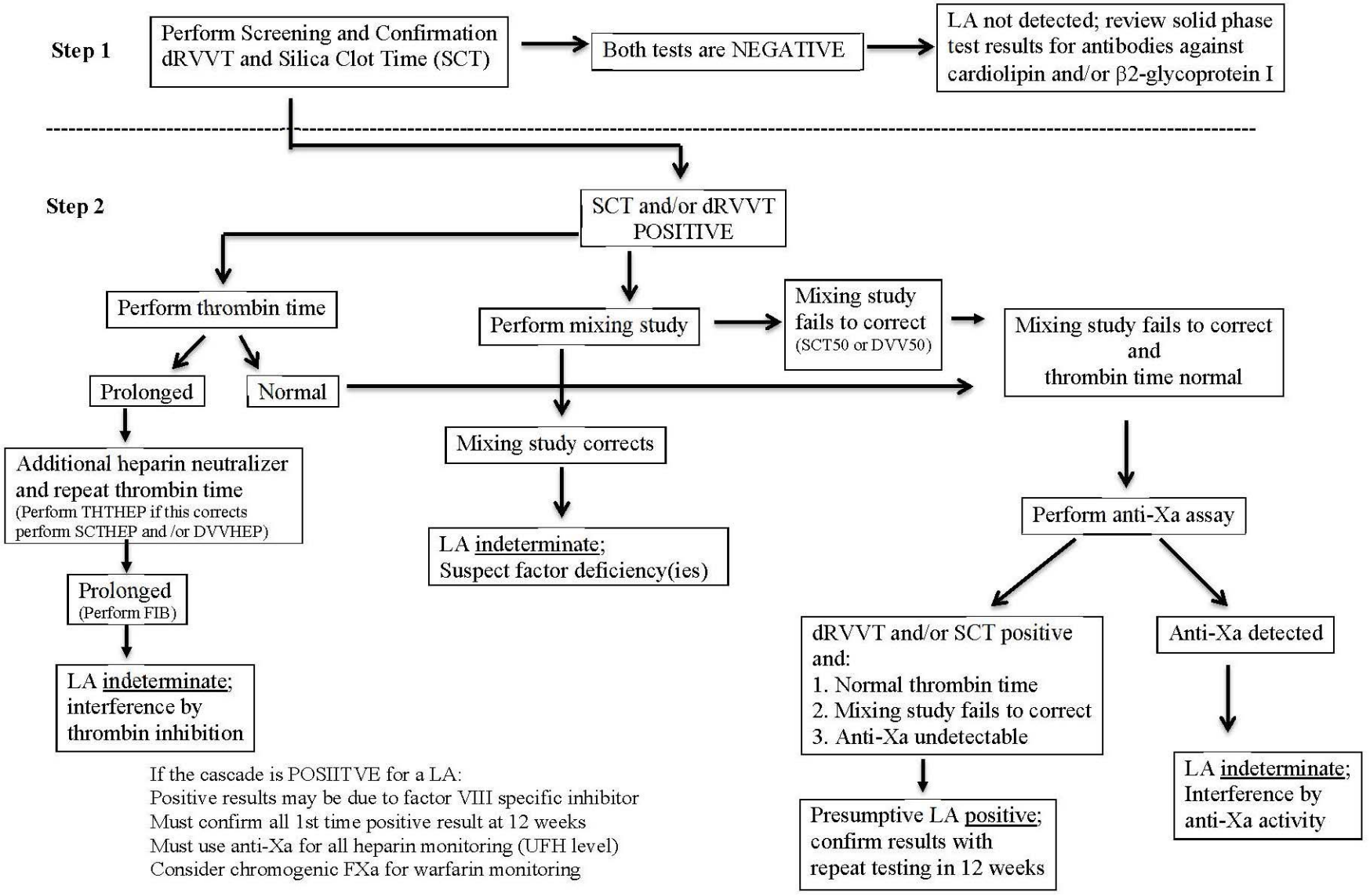
COAGULATION TESTING: LABELING BLUE TOP TUBES

Please take care to place identification labels on top of manufacturer's labels on specimen tubes. The technologist in the lab is required to check the fill level and the sample appearance prior to analysis. The volume of specimen in the tube is critical because there must be a ratio of 9 parts blood to 1-part anticoagulant to produce meaningful results. Sample appearance is important to be sure there is no interference from marked hemolysis or marked lipemia.



Thank you for your help. Please call the Hematology Laboratory at 847-3567 if you have any questions.

Lupus Anticoagulant Cascade



If the cascade is POSIITVE for a LA:
Positive results may be due to factor VIII specific inhibitor
Must confirm all 1st time positive result at 12 weeks
Must use anti-Xa for all heparin monitoring (UFH level)
Consider chromogenic FXa for warfarin monitoring

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