TEST UPDATE

Update to Lupus Anticoagulant Cascade Testing Algorithm

UVMMC

Effective April 15, 2024, the UVMMC Thrombosis and Hemostasis Laboratory will update the testing algorithm for the Lupus Anticoagulant (LA) Cascade. This updated algorithm screens for interfering anticoagulant therapy and aids in appropriate testing and/or interpretation of the LA Cascade test results. There are no changes to the way the cascade is ordered.

Orderable	Epic Code	Atlas Code	Mayo Test ID
Lupus Anticoagulant Cascade	LAB3629	LACASC	FAH5675

The most frequently detected antibodies in anti-phospholipid syndrome (APS) 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.

Consider the following before ordering LA Testing

Clinical Condition	Impact on LA Clot-Based Test	Recommendation
Acute event	False Positive & False Negative	Interpret with caution Avoid testing and/or test following resolution of acute event
Anticoagulant Therapy	False Positive & False Negative	VKA therapy - stop at least 1 - 2 weeks prior to testing with consideration of LMWH bridging If testing while on LMWH therapy, sample should be taken at least 12 hours after last dose (trough level) If feasible, temporarily interrupt DOAC anticoagulation at least 48 hours (longer in patients with renal impairment)
Pregnancy	False Positive & False Negative	Repeat testing at an appropriate time post-delivery to obtain reliable results

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What is changing in the LA Cascade Testing Algorithm?

Mixing studies for the Dilute Russel Viper Venom (DVV) test and the Silica Clot Time (SCT) test will no longer be performed as part of the reflex algorithm of the LA Cascade. Here is the list of reflex-only tests to be discontinued, followed by an updated testing algorithm:

Reflex-only tests to be Discontinued
DVV Screen Mix Time
DVV Screen Mix Ratio
DVV Confirm Mix Time
DVV Confirm Mix Ratio
SCT Screen Mix Time
SCT Screen Mix Ratio
SCT Confirm Mix Time
SCT Confirm Mix Ratio

Updated Algorithm		
Testing	**Always performed?**	**Comments**
Thrombin Time	Yes	*Initial testing*
Qualitative Anti Xa	Yes	*Initial testing*
LA Cascade Summary	Yes	Pathology Interp.
DVV TR Ratio (Normalized)	No	Reflex-only test
SCT TR Ratio (Normalized)	No	Reflex-only test
Dilute Russell Viper Venom Time	No	Reflex-only test
Dilute Russell Viper Venom Time Confirm	No	Reflex-only test
Silica Clotting Time	No	Reflex-only test
Silica Clotting Time Confirm	No	Reflex-only test
Qualitative Anti Xa Hepzymed	No	Reflex-only test
Protime/INR	No	Reflex-only test

Interpretation of Laboratory Test Results

The Thrombosis and Hemostasis Laboratory will continue to provide a written interpretation for all LA Cascade testing. The reflex-only test results, along with the initial testing results, will be included in the LA Cascade Summary.

Medical providers must consider ordering other routine and specialized coagulation 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 DOAC medications such as dabigatran, rivaroxaban, apixaban, and edoxaban. Clinical & Laboratory Standards Institute (CLSI) Guidelines state that patient samples containing heparin may exhibit falsely prolonged clotting times which could lead to incorrect results.

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Cardiolipin and β2-Glycoprotein 1 Antibodies (IgG and IgM)

Please note, the solid phase testing necessary to detect cardiolipin or β2-glycoprotein 1 antibodies is not included in this LA Cascade laboratory testing panel, and these assays must be ordered independently by the medical provider. These solid phase tests require serum samples and cannot be “added on” to the plasma samples used for the LA Cascade.

Orderable	Epic Code	Atlas Code	Mayo Test ID
Phospholipid (Cardiolipin) Antibodies, IgG and IgM, S.	LAB464	CARDLMG	CLPMG
Beta-2 Glycoprotein 1 Antibodies, IgG and IgM, S.	LAB2335	B2GP	B2GMG

For questions or concerns regarding these changes, please contact Dr. Sarah Harm at Sarah.Harm@uvmhealth.org.

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