Test Definition: DRVI4

Dilute Russell's Viper Venom Time (DRVVT) Interpretation (Non-Orderable)

Overview

Useful For

Only orderable as a part of a profile. For more information see DRVI1 / Dilute Russell's Viper Venom Time (DRVVT), with Reflex, Plasma.

Interpreting mixing and confirmation assays for lupus anticoagulants

Method Name

Only orderable as a part of a profile. For more information see DRVI1 / Dilute Russell's Viper Venom Time (DRVVT), with Reflex, Plasma.

Medical Interpretation

NY State Available

Yes

Specimen

Specimen Type

Plasma Na Cit

Specimen Required

Only orderable as a part of a profile. For more information see DRVI1 / Dilute Russell's Viper Venom Time (DRVVT), with Reflex, Plasma.

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Plasma Na Cit	Frozen	14 days	

Clinical & Interpretive

Clinical Information

Lupus anticoagulants (LAs) are immunoglobulins (IgG, IgM, IgA, or a combination of these) of autoimmune type that are specifically directed against antigenic complexes of negatively charged phospholipids (such as phosphatidylserine or phosphatidylethanolamine) and coagulation-related proteins (such as beta-2-glycoprotein I) or clotting factors (including prothrombin [factor II] or factor X) and cause prolongation of phospholipid-dependent clotting time tests due to inhibition.

Lupus anticoagulants are functionally and clinically distinct members of a broader group of antiphospholipid autoantibodies that include immunologically detectable anticardiolipin antibodies or antibodies against other phospholipid-protein complexes. LAs interfere with specific coagulation factor-phospholipid interactions, typically causing prolongation of one or more phospholipid-dependent clotting time tests (eg, activated partial thromboplastin time [APTT], dilute Russell's viper venom time [DRVVT]) due to inhibition. This characteristic in vitro inhibition can be overcome by addition of excess phospholipid.

Because of the heterogeneous nature of LA antibodies, no single coagulation test can identify or exclude all LA. Currently, the International Society on Thrombosis and Haemostasis and the Clinical and Laboratory Standards Institute recommend testing for LA with at least 2 phospholipid-dependent clotting time assays based on different coagulation pathways and principles (eg, lupus-sensitive APTT and DRVVT).

In addition, given the potential for false-positive results in patients on anticoagulants, a profile or panel of coagulation tests is performed, including prothrombin time (PT), APTT, thrombin time (TT) and DRVVT. If the PT, APTT, or DRVVT are prolonged, additional testing may include mixing tests with normal plasma (to evaluate for inhibition) and the use of excess phospholipid in appropriate assay systems to evaluate for phospholipid-dependent inhibition. Additional reflexive testing helps determine presence or absence of anticoagulants and inhibitors to other factors.

The diagnosis of LA requires performance and interpretation of complex coagulation testing as well as correlation with available clinical information including evidence of persistence of LA over time (> or =12 weeks).

The venom obtained from Russell's viper *(Vipera russelli)* contains enzymes that directly activate coagulation factors V and X, bypassing the activation of factors VII, VIII, IX, XI, and XII, and therefore, the effect of deficiencies or inhibitors of these factors. Diluting the phospholipid necessary for the clotting factor interactions increases the sensitivity to LA and the likelihood of identifying a phospholipid-dependent inhibitor that may not be detected by other coagulation tests with higher phospholipid content (eg, LA-insensitive APTT reagents).

Dilute Russell's viper venom time testing is used in conjunction with other appropriate coagulation tests (reflexive testing panels) to assist in detection and confirmation of LAs or to help exclude their presence.

The DRVVT may be abnormally prolonged (DRVVT screen ratio > or =1.20) by LAs as well as coagulation factor deficiencies, anticoagulant effects, or other types of coagulation factor inhibitors.

Specimens with abnormal results (DRVVT screen ratio > or =1.20) are subjected to reflexive testing. With reflexive testing, the sensitivity of DRVVT testing for LA diagnosis is approximately 65% to 70%, and the specificity is 95% or higher.

It is advisable to use the DRVVT screen, mixing study, and confirmation ratio results in conjunction with other appropriate coagulation tests (reflexive testing panels) to diagnose or exclude LA.

Although LAs cause prolonged clotting times in vitro, there is a strong association with thrombosis risk. However, not all patients with persisting LAs develop thrombosis.

Reference Values

Only orderable as a part of a profile. For more information see DRVI1 / Dilute Russell's Viper Venom Time (DRVVT), with Reflex, Plasma.

An interpretive comment will be provided.

Interpretation

A normal dilute Russell's viper venom time (DRVVT) screen ratio (<1.20) indicates that lupus anticoagulant (LA) is not present or not detectable by this method (but might be detected with other methods).

An abnormal DRVVT screen ratio (DRVVT screen ratio > or =1.20) may suggest presence of LA; however, other possibilities include:
-Deficiencies or dysfunction of factors I (fibrinogen), II, V, or X, congenital or acquired
-Inhibitors of factor V, or occasionally by inhibitors of factor VIII, or other specific or nonspecific inhibitors
-Anticoagulation therapy effects (see Cautions)

Further evaluation consists of performing mixing studies with an equal volume of normal pooled plasma (DRVVT 1:1 mix) to investigate the possibility of coagulation factor deficiency (suggested by DRVVT mix ratio <1.20) and to evaluate inhibition (suggested by DRVVT mix ratio > or =1.20) and mixing patient plasma with DRVVT reagent enriched in phospholipid (DRVVT confirmatory reagent) (DRVVT mix and DRVVT confirmation ratios).

Possible combination of results includes the following:
-DRVVT screen ratio > or =1.20, DRVVT mix ratio <1.20, and DRVVT confirmation ratio <1.20:
No evidence of LA. These data may reflect anticoagulation therapy effects or other (congenital or acquired) coagulopathy.
-DRVVT screen ratio > or =1.20, DRVVT mix ratio > or =1.20, and DRVVT confirmation ratio <1.20:
The prolonged and inhibited DRVVT (DRVVT screen and mix ratios) may reflect presence of a specific factor inhibitor (eg, factor V inhibitor), anticoagulation therapy effects or other nonspecific inhibitors as can be seen with monoclonal protein disorders, lymphoproliferative disease etc. Although LA cannot be conclusively excluded, the DRVVT confirmation ratio of < or =1.20 makes this less likely.
-DRVVT screen ratio > or =1.20, DRVVT mix ratio <1.20, and DRVVT confirmation ratio > or =1.20:
Although mixing study of the prolonged DRVVT screen and mix ratios provides no evidence of inhibition, additional phospholipid shortens the clotting time (DRVVT confirmation ratio), suggesting presence of LA.
-DRVVT screen ratio > or =1.20, DRVVT mix ratio > or =1.20, and DRVVT confirmation ratio > or =1.20:
The data are consistent with presence of LA, provided anticoagulant effect can be excluded (see Cautions)

Dilute Russell's viper venom assays ordered as a single, stand-alone test should be interpreted within patient clinical context and close attention to medication use by patient (see Cautions).

Cautions

Residual platelets in frozen-thawed plasma can decrease sensitivity and specificity of lupus anticoagulants (LAs) testing (false-negative results). Specimens that are to be frozen before testing must be centrifuged twice to remove as many of the platelets as possible before freezing.

Anticoagulation therapy effects such as warfarin (especially when the effect is supratherapeutic), excess heparin, direct thrombin inhibitors (eg, dabigatran [Pradaxa]), argatroban [Ancova], bivalirudin [Angiomax]), direct factor Xa inhibitors (eg, rivaroxaban [Xarelto], apixaban [Eliquis], edoxaban [Savaysa]) may result in a false-positive assay performance for LA. Clinical correlation and repeat testing remote (>1 week) from anticoagulation therapy is suggested.

Although the dilute Russell's viper venom time (DRVVT) reagents contain a heparin inhibitor (Polybrene) that is sufficient for neutralization of heparin (up to 1-2 U/mL), the results may not necessarily represent what would occur if no heparin were present in the specimen. Therefore, DRVVT results from heparinized plasma should be interpreted with caution.

Dilute Russell's viper venom assays, when performed in isolation, will not distinguish LA from heparin or inhibitors of factors V or VIII, which may cause false-positive results of LA testing.

Excess heparin or inhibitors of factor V or VIII may cause false-positive results of LA testing, depending on the types of coagulation testing performed.

Lupus anticoagulant diagnosis does not have definite predictive value for associated clinical complications such as thromboembolic problems or fetal loss.

The DRVVT test will not detect all LAs. Some LAs may only be detectable by other tests such as the Hexagonal LA, activated partial thromboplastin time, platelet neutralization procedure, or other methods.

Persistence of LA over time (12 weeks or more between positive testing results) is a clinically important criterion for the antiphospholipid antibody syndrome diagnosis.

Clinical Reference

1. Proven A, Bartlett RP, Moder KG, et al. Clinical importance of positive test results for lupus anticoagulant and anticardiolipin antibodies. Mayo Clin Proc. 2004;79(4):467-475
2. Gastineau DA, Kazmier FJ, Nichols WL, Bowie EJ. Lupus anticoagulant: an analysis of the clinical and laboratory features of 219 cases. Am J Hematol. 1985;19(3):265-275
3. Brandt JT, Triplett DA, Alving B, Scharrer I. Criteria for the diagnosis of lupus anticoagulants: an update. On behalf of the Subcommittee on Lupus Anticoagulant/Antiphospholipid Antibody of the Scientific and Standardisation Committee of the ISTH. Thromb Haemost. 1995;74(4):1185-1190
4. Arnout J, Vermylen J. Current status and implications of autoimmune antiphospholipid antibodies in relation to thrombotic disease. J Thromb Haemost. 2003;1(5):931-942
5. Pengo V, Tripodi A, Reber G, et al. Update of the guidelines for lupus anticoagulant detection. Subcommittee on Lupus Anticoagulant/Antiphospholipid Antibody of the Scientific and Standardisation Committee of the International Society on Thrombosis and Haemostasis. J Thromb Haemost. 2009;7(10):1737-1740. doi:10.1111/j.1538-7836.2009.03555.x
6. Clinical and Laboratory Standards Institute (CLSI). Laboratory Testing for Lupus Anticoagulant; Approved Guideline. CLSI document H60-A. CLSI; 2014
7. Favaloro EJ and Lippi G. eds. Hemostasis and Thrombosis, Methods and Protocols. Humana Press; 2017

Performance

Test Definition: DRVI4

Dilute Russell's Viper Venom Time (DRVVT) Interpretation (Non-Orderable)

Method Description
A coagulation expert (clinician or hematopathologist) reviews the laboratory data, and an interpretive report is issued.

PDF Report
No

Day(s) Performed
Monday through Friday

Report Available
2 days

Performing Laboratory Location
Mayo Clinic Laboratories - Rochester Main Campus

Fees & Codes

Fees
- Authorized users can sign in to Test Prices for detailed fee information.
- Clients without access to Test Prices can contact Customer Service 24 hours a day, seven days a week.
- Prospective clients should contact their account representative. For assistance, contact Customer Service.

Test Classification
Not Applicable

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
DRVI4	DRVVT Interpretation	50008-2

Result ID	Test Result Name	Result LOINC® Value
DRVI4	DRVVT Interpretation	50008-2