MAYO CLINIC LABORATORIES

Test Definition: DRVI1

Dilute Russell's Viper Venom Time (DRVVT), with Reflex, Plasma

Overview

Useful For

Detecting and confirming or helping to exclude the presence of lupus anticoagulants (LAs)

Identifying LAs that do not prolong the activated partial thromboplastin time (APTT)

Evaluating unexplained prolongation of the APTT or prothrombin time clotting tests

Distinguishing LA from a specific coagulation factor inhibitor or coagulation factor deficiencies

Reflex Tests

Test Id	Reporting Name	Available Separately	Always Performed
DRVI2	DRVVT Mix Ratio	No	No
DRVI3	DRVVT Confirmation Ratio	No	No

Additional Tests

Test Id	Reporting Name	Available Separately	Always Performed
DRVI4	DRVVT Interpretation	No	Yes

Testing Algorithm

If dilute Russell's viper venom time (DRVVT) ratio is 1.20 or above, then DRVVT mix and DRVVT confirmation will be performed at an additional charge.

If DRVVT ratio is less than 1.20, the DRVVT mix and DRVVT confirmation will not be performed.

A DRVVT interpretation will always be performed.

Special Instructions

- Coagulation Guidelines for Specimen Handling and Processing

Method Name

DRVI4: Medical Interpretation
DRVI1, DRVI2, DRVI3: Optical Clot-Based

NY State Available

Yes

Specimen

Specimen Type
Plasma Na Cit

Ordering Guidance
Because no single coagulation test can identify or exclude all lupus anticoagulants (LA), and because of the complexity of testing LA, one of the following Coagulation Consultation reflexive panel procedures are recommended if clinically indicated:
ALUPP / Lupus Anticoagulant Profile, Plasma
AATHR / Thrombophilia Profile, Plasma and Whole Blood
APROL / Prolonged Clot Time Profile, Plasma

Additional Testing Requirements
Serum anticardiolipin antibody testing (CLPMG / Phospholipid [Cardiolipin] Antibodies, IgG and IgM, Serum) and anti-beta-2 glycoprotein I (B2GMG / Beta-2 Glycoprotein 1 Antibodies, IgG and IgM, Serum) antibody testing should also be performed in conjunction with coagulation-based testing for lupus anticoagulants to enhance detection of different types of antiphospholipid antibodies.

Shipping Instructions
Send specimens in the same shipping container.

Specimen Required
Specimen Type: Platelet-poor plasma
Collection Container/Tube: Light-blue top (3.2% sodium citrate)
Submission Container/Tube: 13-mm x 75-mm, 5-mL, plastic vial (polypropylene preferred)
Specimen Volume: 1 mL Platelet poor plasma
Collection Instructions:
1. For complete instructions, see Coagulation Guidelines for Specimen Handling and Processing.
2. Centrifuge, transfer all plasma into a plastic vial, and centrifuge plasma again.
3. Aliquot into a separate plastic vial, leaving 0.25 mL in the bottom of the centrifuged vial.
4. Immediately freeze plasma (no longer than 4 hours after collection) at -20 degrees C or, ideally, -40 degrees C or below.
Additional Information:
1. Double-centrifuged specimen is critical for accurate results as platelet contamination may cause spurious results.
2. Each coagulation assay requested should have its own vial.

Forms
If not ordering electronically, complete, print, and send a Coagulation Test Request (T753) with the specimen.

Specimen Minimum Volume
Platelet poor plasma 0.5 mL

Reject Due To

Gross hemolysis	Reject
Gross lipemia	Reject
Gross icterus	Reject

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 (CLSI) 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 testing is recommended, 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 the presence or absence of anticoagulants or 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 the 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 that have a 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 LA or 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 (see Testing Algorithm). With reflexive testing algorithm, 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

Dilute Russell's viper venom time screen ratio:
<1.20
Normal ranges for children: Not clearly established but similar to normal ranges for adults, except for newborn infants whose results may not reach adult values until age 3 to 6 months.

Interpretation

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

Abnormal DRVVT screen ratio (DRVVT screen ratio > or =1.20) may suggest the 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 confirm ratios).

Possible combinations of results include the following:
-DRVVT screen ratio > or =1.20, DRVVT mix ratio <1.20, and DRVVT confirm ratio <1.20:

No evidence of LA. This 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 confirm 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 confirm ratio of < or =1.20 makes this less likely.
-DRVVT screen ratio > or =1.20, DRVVT mix ratio <1.20, and DRVVT confirm 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 confirm ratio), suggesting presence of LA.
-DRVVT screen ratio > or =1.20, DRVVT mix ratio > or =1.20, and DRVVT confirm 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 single, stand-alone tests 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 (LA) 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.

The dilute Russell's viper venom time (DRVVT) test will not detect all LA. Some LA may only be detectable by other tests such as the Hexagonal LA, activated partial thromboplastin time, platelet neutralization procedure, or other methods.

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 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 factors 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.

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, Sharrer I. Criteria for the diagnosis of lupus anticoagulant: 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, Rand JH, 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;7:1737-1740. 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

Method Description

The dilute Russell's viper venom time (DRVVT) screening assay is performed on the Instrumentation Laboratory ACL TOP. Patient plasma is incubated for a specified time, then combined with a DRVVT screening reagent containing Russell's viper venom, phospholipids, heparin neutralizing agents, calcium, buffers, and stabilizers to trigger the coagulation process. Subsequently, the time to clot formation is measured optically using a wavelength of 671 nm. The patient DRVVT screening clotting time is normalized by dividing the patient result by the mean DRVVT screening clotting time of normal pooled plasma to yield a ratio (DRVVT screen ratio).

Patient samples with a prolonged DRVVT (DRVVT screen ratio > or =1.20) are further studied by adding an equal volume of normal pooled plasma (platelet-depleted) and repeating the DRVVT test procedure, with mathematical normalization, to yield the DRVVT mix (1:1) ratio and the DRVVT test using DRVVT confirmatory reagent (enriched in phospholipid), and results are expressed as the quotient obtained from dividing the patient DRVVT screening clotting time by the patient DRVVT confirmatory clotting time (DRVVT confirm ratio).(Thiagarajan P, Pengo V, Shapiro SS. The use of the dilute Russell's viper venom time for the diagnosis of lupus anticoagulants. Blood.1986;68[4]:869-874; package inserts: CRYOcheck LA CHECK DRVVT. Precision BioLogic; 01/2023; CRYOcheck LA SURE DRVVT. Precision BioLogic; 01/2023)

PDF Report

No

Day(s) Performed

Monday through Friday

Report Available

1 to 4 days

Specimen Retention Time
7 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
This test has been cleared, approved, or is exempt by the US Food and Drug Administration and is used per manufacturer's instructions. Performance characteristics were verified by Mayo Clinic in a manner consistent with CLIA requirements.

CPT Code Information
85613
85613 (if appropriate)
85613 (if appropriate)

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
DRVI1	DRVVT Screen Ratio, w/Reflex, P	15359-3

Result ID	Test Result Name	Result LOINC® Value
RVRI1	DRVVT Screen Ratio	15359-3