USEFUL FOR

- Detecting and confirming or helping to exclude the presence of lupus anticoagulants (LA)
- Identifying LA that do not prolong the activated partial thromboplastin time (APTT)
- Evaluating unexplained prolongation of the APTT or prothrombin time clotting tests

CLINICAL INFORMATION

Lupus anticoagulants (LA) 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 (beta-2-GPI) or clotting factors including prothrombin (factor II) or factor X, and cause prolongation of phospholipid-dependent clotting time tests due to inhibition.

LA are functionally and clinically distinct members of a broader group of antiphospholipid autoantibodies (APA) that includes immunologically detectable anticardiolipin antibodies or antibodies against other phospholipid-protein complexes. LA interfere with specific coagulation factor-phospholipid interactions, typically causing prolongation of 1 or more phospholipid-dependent clotting time tests (eg, activated partial thromboplastin time: APTT, dilute Russell 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 the prothrombin time (PT), APTT, thrombin time (TT), and the 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 (≥12 weeks).

REFERENCE VALUES

Dilute Russell viper venom time screen ratio <1.2

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 3 to 6 months of age.

ANALYTIC TIME

1 day
The venom obtained from the Russell 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).

The DRVVT screen ratio test is one of several available in vitro tests that may be used to screen and confirm the presence of LA or to help exclude LA.

The DRVVT may be abnormally prolonged (DRVVT screen ratio ≥1.2) by LA as well as coagulation factor deficiencies, anticoagulant effects, or other types of coagulation factor inhibitors.

Specimens with abnormal results (DRVVT screen ratio ≥1.2) are subjected to reflexive testing (DRVVT mix and confirmation ratios) as described in the Testing Algorithm (also see Interpretation).

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

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

**CLINICAL REFERENCE**