Lupus Anticoagulant Reflex Panel

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Lupus anticoagulant (LA) is an antiphospholipid antibody (aPL) autoantibody that binds to phospholipid-binding proteins, beta-2 glycoprotein I, and prothrombin, leading to a prothrombotic state. LA is associated with a range of adverse medical events, such as thrombosis and loss of pregnancy. LA can be transient (eg, due to certain medications or infections) and may not show clinical symptoms in all cases. No single test currently exists for the detection of LA; instead, a combination of clot-based tests with appropriate reflexive steps are recommended. Persistently positive LA, anticardiolipin (aCL) IgG or IgM, or anti-beta-2 glycoprotein 1 (anti-β2GP1) IgG or IgM results (ie, consecutively positive on at least two occasions 12 weeks apart) fulfill the laboratory classification criteria for antiphospholipid syndrome (APS); they are more likely than transiently positive LA to be associated with clinical symptoms.[1,2,3]

Featured ARUP Testing

Lupus Anticoagulant Reflex Panel 3017009

Method: Electromagnetic Mechanical Clot Detection/Chromogenic Assay

Use to aid in the evaluation of unexplained prolonged activated partial thromboplastin time (aPTT) or for patients with a significant probability of having antiphospholipid syndrome (APS). To assess for APS, order with anticardiolipin (aCL) antibodies, IgG and IgM, and anti-beta-2 glycoprotein 1 (anti-β2GP1) antibodies, IgG and IgM.

Test Description

ARUP's Lupus Anticoagulant Reflex Panel includes a combination of two clot-based screening assays (activated partial thromboplastin time [aPTT] and dilute Russell viper venom time [dRVVT]), with reflexively performed mixing and confirmation steps, as well as anticoagulant identification and neutralization (as applicable).

Anticoagulant Neutralization

Activated charcoal-based direct oral anticoagulant (DOAC) neutralizing compounds (eg, DOAC-Stop) and heparinase (eg, Hepzyme) are included in the panel in cases where screening assays suggest the presence of anticoagulant medication. However, if clinically feasible, LA testing should be performed before starting anticoagulation therapy or after its completion.

Anticoagulant	Comments
Direct Xa Inhibitors	DOAC-Stop neutralizes oral direct Xa inhibitors (rivaroxaban, apixaban, edoxaban) at concentrations up to 500 ng/mL It is recommended to wait 48-72 hrs after discontinuing an oral direct Xa inhibitor before drawing samples for LA testing
DTIs	DOAC-Stop neutralizes the oral DTI dabigatran and may neutralize parenteral DTIs (argatroban and hirudin analogues) It is recommended to wait 4-8 hrs after discontinuing parenteral DTI infusion before drawing samples for LA testing It is recommended to wait 48-72 hrs after discontinuing an oral DTI before drawing samples for LA testing
LMWH	Hepzyme neutralizes LMWH but may be less effective compared with its neutralization of UFH It is recommended to wait 24-48 hrs after discontinuing LMWH injections before drawing samples for LA testing
UFH	Hepzyme neutralizes typical therapeutic concentrations (≤2 units/mL) of UFH. Higher concentrations of UFH will not be completely neutralized and will appear as an inhibitor in mixing studies It is recommended to wait 4-8 hrs after discontinuing a UFH infusion before drawing samples for LA testing

DTI, direct thrombin inhibitor; LMWH, low molecular weight heparin; UFH, unfractionated heparin

Test Interpretation

Sensitivity/Specificity

Varies. Refer to Results for reference intervals.

Results

Panel Component	Result If Performed (Reported As)	Reference Interval
Prothrombin time	Time in seconds	12.0-15.5 s
PTT-LA ratio	Ratio	≤1.20
dRVVT screen ratio	Ratio	≤1.20
Anti-Xa qualitative interpretation	Present or not present	Not present
Thrombin time	Time in seconds	≤19.5 s
Anticoagulant medication neutralization	DOAC-Stop or Hepzyme	Not performed
Neutralized PTT-LA ratio	Ratio	≤1.20
Neutralized dRVVT screen ratio	Ratio	≤1.20
dRVVT 1:1 mix ratio	Ratio	≤1.20
dRVVT confirmation ratio	Ratio	≤1.20
Hexagonal phospholipid confirmation	Time in seconds (delta)	≤7.9 s
LA interpretation	LA detected or LA not detected with a narrative comment	N/A

Limitations

- Results should be interpreted within the context of a patient's complete clinical picture.
- The following factors may result in test interference or spurious results:
  - Acute phase reactions due to pregnancy, malignancy, inflammatory or infectious states, or trauma
  - Liver disease
  - Anticoagulant medications in concentrations exceeding the capacity of neutralizing reagents (heparins, DOACs)
  - Warfarin effect
  - Residual platelets (≥10,000 platelets/uL) in the plasma sample
  - Specific factor antibodies directed against clotting factors involved in the intrinsic or common pathways

References

1. Devreese KMJ, de Groot PG, de Laat B, et al. Guidance from the Scientific and Standardization Committee for lupus anticoagulant/antiphospholipid antibodies of the International Society on Thrombosis and Haemostasis: update of the guidelines for lupus anticoagulant detection and interpretation. *J Thromb Haemost*. 2020;18(11):2828-2839.

2. Vandevelde A, Devreese KMJ. Laboratory diagnosis of antiphospholipid syndrome: insights and hindrances. *J Clin Med*. 2022;11(8):2164.

3. Barbhaiya M, Zuily S, Naden R, et al. 2023 ACR/EULAR antiphospholipid syndrome classification criteria. *Ann Rheum Dis*. 2023;82:1258-1270.

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