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Antiphospholipid Syndrome

Antiphospholipid Syndrome (APS) is an autoimmune condition with clinical manifestations that include arterial and venous thrombosis, multiple spontaneous fetal loss, neurological problems or thrombocytopenia. The diagnosis of APS is difficult and relies upon the association of clinical symptoms with the laboratory detection of anti-phospholipid antibodies. The classification criteria for APS were first formulated by the ISTH scientific subcommittee on lupus anticoagulants/APS in 1995 in Sapporo, Japan.^{1,2} In 2006 at a workshop before the Eleventh International Congress on Antiphospholipid antibodies in Sydney, Australia, the clinical and laboratory criteria for APS were updated.³

Lupus Anticoagulants and Clotting Assays

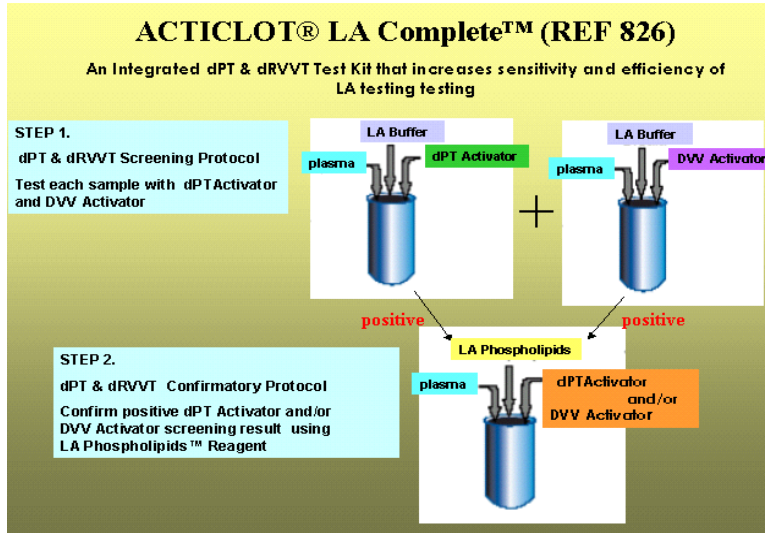
Lupus anticoagulants are antiphospholipid antibodies which cause prolongation of clotting in phospholipid-sensitive clotting assays such as dilute Russell viper venom time (dRVVT), activated partial thromboplastin time (aPTT), the kaolin clotting time (KCT), and the dilute prothrombin time (dPT) tests. The presence of Lupus Anticoagulants is one of the most difficult and challenging determinations for the coagulation laboratory as no one single test has proven to be 100% accurate and specific. The ISTH guidelines for LA testing recommend:

- 1) Performing at least two clot-based screening assays using clotting assays with different assay principles
- 2) Determination of LA on two or more occasions at least twelve weeks apart
- 3) Confirmation of the phospholipid-dependence of the autoantibody
- 4) Methods to rule out inhibitors and factor deficiencies using mixing studies
- 5) Eliminate presence of heparin using specific neutralizers

In LA clot-based assays, clotting can be initiated through the intrinsic pathway, the common pathway or the extrinsic pathway. Many studies have shown that the most commonly used type of LA assays such as activated partial thromboplastin time (aPTT) which operates through the intrinsic pathway and the dilute Russell's viper venom test (dRVVT) which operates through the common pathway, do not identify the same subset of LA samples. Many LA samples may test positive on only one of the two assays. However, a significant number of LAs are missed using a panel comprising dRVVT and aPTT tests. Several studies have shown that 10-20% of LA samples are identified only by the dilute prothrombin time (dPT) assay which initiates coagulation via the extrinsic (tissue factor) pathway.⁶ Thus, an optimal panel of LA tests should include all three of the major LA tests – aPTT, dRVVT and dPT in order to avoid misdiagnosing many LAs.

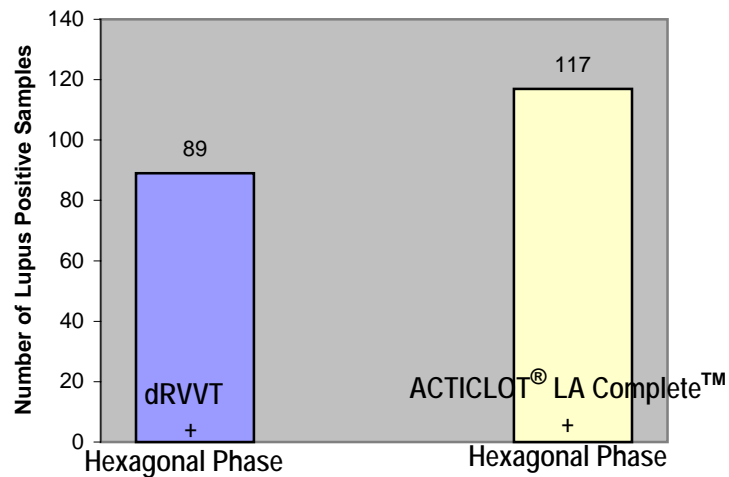
ACTICLOT® LA Complete™

ACTICLOT® LA Complete™ represents a significant product advancement in LA testing. ACTICLOT® LA Complete™ is a fully integrated dPT and dRVVT test system that can increase efficiency, reduce turnaround time and decrease labor costs. With this test, samples are screened in one run for LA using dPT Activator and our tried and true DVV test (dRVVT). Samples testing positive with either or both screening reagents can then be confirmed using LA Phospholipids Reagent™. Thus, in one instrument cycle you can satisfy most of the ISTH guidelines for LA testing – multiple tests, different principles and confirm phospholipids dependence of a positive screen.



Clinical Study

A prospective clinical study was performed at Duke University Medical School whereby 529 consecutive patient samples were tested for lupus anticoagulants using aPTT/hexagonal phase, dRVVT [DVV *test*/DVV *confirm*] and ACTICLOT® LA Complete™ clot-based assays. The results showed that the LA panel comprising ACTICLOT® LA Complete™ (dPT + dRVVT) and aPTT/Hexagonal phase tests identified 31% greater number of lupus anticoagulant samples in routine screening than a panel consisting of dRVVT + aPTT/Hexagonal phase tests.



Conclusion

ACTICLOT® LA Complete™ is simple to perform, increases LA testing efficiency, saves labor time and decreases testing costs. By incorporating ACTICLOT® LA Complete™ in your LA testing panel, you will exceed ISTH testing guidelines for lupus anticoagulants. You can also be confident that you no longer are missing lupus anticoagulant positive samples in your daily LA testing routine.

Selected References

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4. Swadzba J., Iwaniec T, Szczeklik A and Musial J. Revised classification criteria for antiphospholipid syndrome and the thrombotic risk in patients with autoimmune diseases. *J Thromb Haemost.* 5, 1883-1889, 2007.
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