Lupus Anticoagulants (LA) / Antiphospholipid antibodies (APA)

● Antiphospholipid antibodies are a heterogeneous family of antibodies directed against proteins bound to negatively charged phospholipids. Lupus-type inhibitors belong to this family of antibodies as do anticardiolipin antibodies. The presence of antiphospholipid antibodies is a biological marker for antiphospholipid syndrome (APS).

● APS is an autoimmune disease associated with high risk for thrombosis, recurrent spontaneous miscarriage, thrombocytopenia and numerous other clinical manifestations.

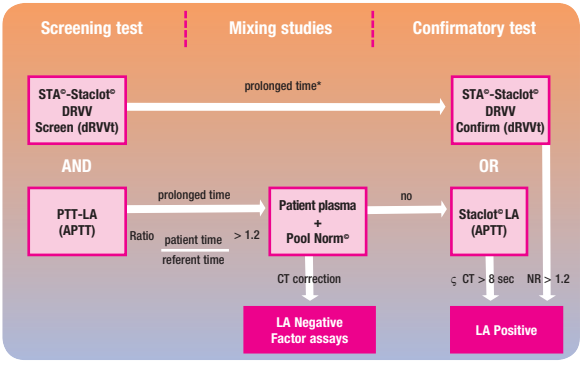
● Lupus inhibitor is also known as «antiprothrombinase anticoagulant antibody» or «lupus anticoagulant» (LA).

- LA is an acquired abnormality affecting between 1 and 5% of the general population. However, only 15 to 20% of these individuals are positive for control testing performed several months afterwards.
- *In vitro*, LA results in prolonged coagulation times in phospholipid-dependent tests (e.g. aPTT or PT as well as certain APCR tests). Diluted Russell's viper venom time (dRVVT) is a specific test used for LA screening.
- *In vivo*, LA is associated with a risk of thrombosis that may result in obstetric, neurological stroke, renal or pulmonary complications.

● A single test is not sufficient to allow the diagnosis of this syndrome.

● In some patients, transient antiphospholipid antibodies may be detected due to infection or to another treatment, despite the absence of any clinical signs.

Diagnostic decision tree for screening for LA according to ISTH recommendations (1)



NR: Normalized Ratio;
CT: Clotting Time
* If OAT patient, mix 1:1 plasma patient - Pool Norm®
** according to Rosner Index or ICA calculation (1)

Laboratory diagnosis

Diagnosis may only be made on the basis of two types of test: immunological tests with screening for APA and/or coagulation tests specific for LA.
The recommendations of the «Scientific Subcommittees of the International Society on Thrombosis and Haemostasis» (ISTH) are as follows:

1) Lupus Anticoagulants (LA)
Must be detected in plasma on at least two occasions separated by a minimum interval of 12 weeks:

- **Screening step:** detection of increased coagulation time during a phospholipid-dependent test;
  - At least 2 screening tests must be performed before LA can be ruled out:
    - The first-line test is the DRVV test.
    - The second-line test consists of sensitised aPTT containing silica activator and a low concentration of phospholipids.
- **Identification step for the presence of a coagulation inhibitor:** 50/50 mix of patient + control (a commercially available pool may be used).
- **Confirmation step indicating that the inhibition** is phospholipid-dependent; the selected test contains a high phospholipid concentration. It must be based on the same principle as the screening test.

Exclusion of associated clotting disorder.

2) Anticardiolipin antibody (aCL) (IgG and/or IgM)
May be present in serum or plasma, in moderate to high concentrations (e.g. > 40 GPL or MPL, or > 99th percentile), on at least two occasions, separated by a minimum interval of 12 weeks, determined using a standardised ELISA method.

3) Anti-ß2 glycoprotein I antibodies (IgG and/or IgM)
May be present in serum or plasma (titre > 99th percentile), on one or two occasions, separated by a minimum interval of 12 weeks, determined using a standardised ELISA method, in accordance with the recommended operating procedure.

Bibliography:
- Pengo A, Update of the guidelines for lupus anticoagulant detection. J. Thromb Haemost. 2009; 7: 137-40.
- Miyakis S et al. International consensus statement on an update of the classification criteria for definite anti-phospholipid syndrome (APS). J Thromb Haemost. 2006; 4: 295-306.