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THE LUPUS ANTICOAGULANT PARADOX

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Introduction:

Lupus Anticoagulant (LA) is by far the most enigmatic antibody population in patients with antiphospholipid syndrome, that was an unsolved paradox only 50 years ago. In 1952, Conley and Hartman described patients with bleeding symptoms, whose plasma lengthened the blood clotting time and they failed to correct the addition of normal plasma. Other patients have been reported, and in 1972 the term "lupus anticoagulant" was coined, as the apparent coagulation inhibitor was observed in patients with systemic lupus erythematosus (SLE). However, the notion of "lupus anticoagulant" has proven to be wrong, as LA is often found in plasma in patients with clinical conditions other than SLE and it is associated with thromboembolic events, which may occur in healthy individuals.

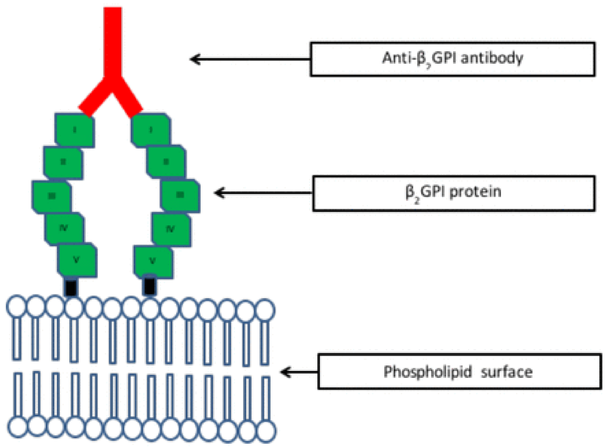
Purpose:

The goal of the research is to present the reasons that cause the respective prolongation of the coagulation time induced by LA to be mostly associated with thrombosis, than with a tendency to bleed.

Keywords: lupus anticoagulant, prothrombin, thrombosis.

Material and methods:

For the research was studied the specialty literature on biochemical perspectives and mechanisms of The lupus anticoagulant paradox.



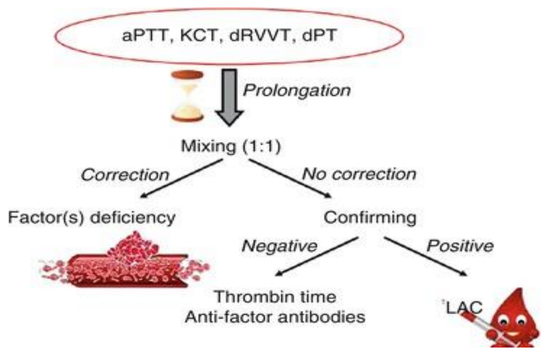
Laboratory Diagnosis of the Lupus Anticoagulant

β_2GPI and antibody. β_2GPI and antibody to β_2GPI binding to a phospholipid surface. B2GPI consists of 5 homologous domains. Domain V binds to the anionic phospholipid surface. The anti-β_2GPI antibody binds to domain I.

Results:

Lupus anticoagulants are a heterogeneous class of immunoglobulins (predominantly IgG autoantibodies and, rarely, IgM), which bind specifically to the epitopes of negatively charged plasma phospholipid binding proteins, prothrombin, beta2-glycoprotein I (most commonly, domain D I of the molecule is involved) or annexin V, inhibiting phospholipid-dependent coagulation *in vitro*. LA forms an APLA subgroup that disrupts the *in vitro* assembly of the prothrombinase complex (factors Xa, Va and prothrombin in the complex on phospholipid membranes), leading to prolongation of aPTT, diluted Russell viper venom time (dRVVT), coagulation time kaolin plasma and rarely prothrombin time. *In vivo*, the mechanism of thrombosis is explained by Ig G binding to phospholipids, a phenomenon that is essential for the degradation of the normal effects of protein C and protein S, thus changing the balance in favor of thrombus formation. There are many mechanisms for inducing LA, including infections, oxidative stress, and major stress, such as surgery or trauma. All of these stressors help expose phospholipids, which eventually allow antibodies to attach. At this turn, this leads to intravascular coagulation and thrombus formation.

The prevalence of thrombosis in patients with lupus anticoagulants is 24-36%; deep limb thrombosis and pulmonary embolism predominate. Patients with recurrent miscarriages have lupus anticoagulants in approximately 10% of cases. The prevalence of LA in patients with SLE is attested only in 5-10% of cases.



Conclusions:

Lupus anticoagulant has procoagulant properties *in vivo* and prolongs coagulation times addicted to phospholipid *in vitro*. Extended in vitro coagulation time may be mistaken as a bleeding disorder. Different thromboplastin reagents and plasma mixing assays, as well as independent thromboplastin coagulation assays may be useful to differentiate in vitro changes associated with LA from in vivo coagulation factor deficiency.