Correlation Between Antiphospholipid Antibodies And Complications of P.I.H

By

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بسم الله الرحمن الرحيم

وما أوتيتم من العلم إلا قليلا

صدق الله العظيم

الإسراء آية ٨٥

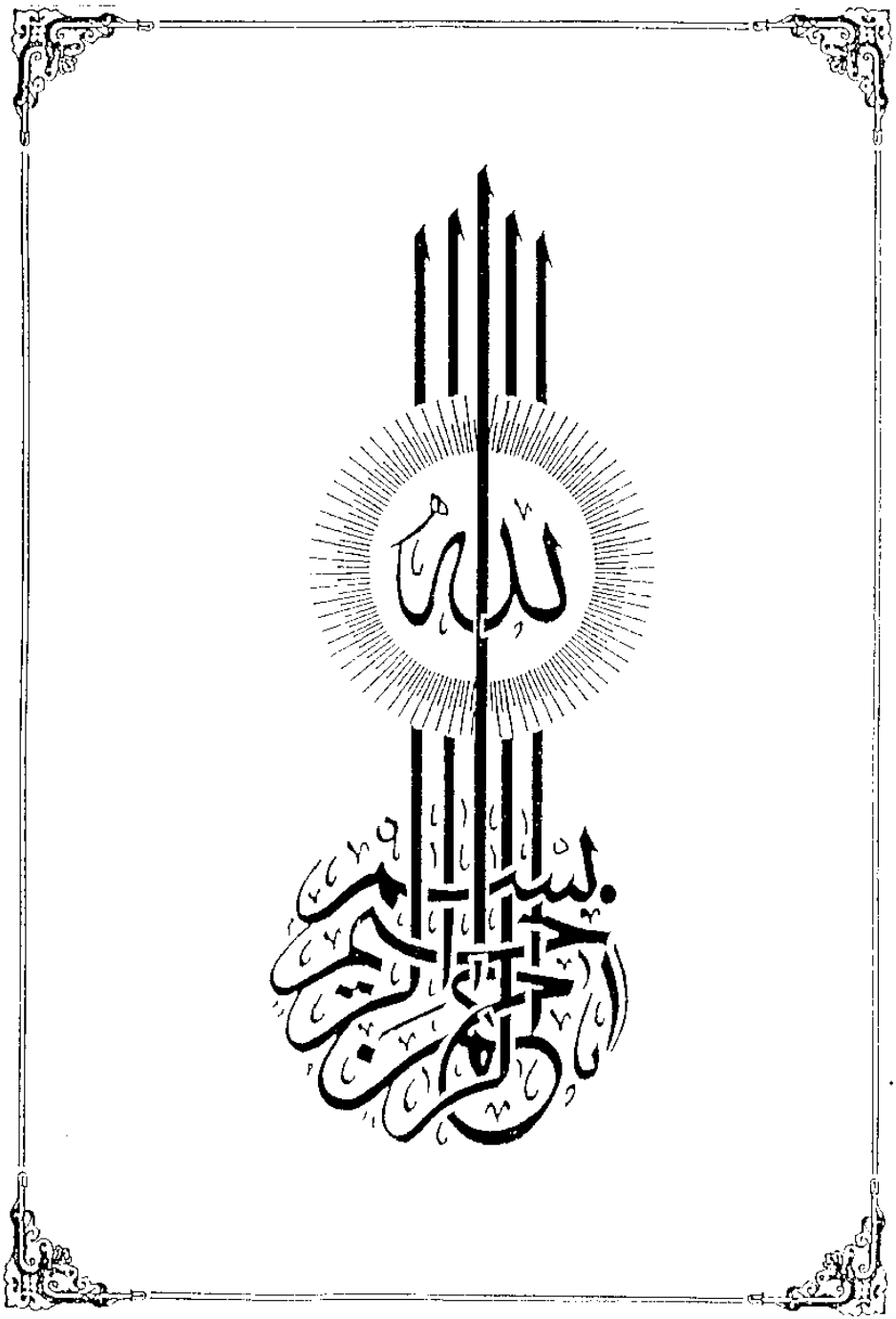

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Table of Contents

INTRODUCTION

Circulating antibodies to negatively charged phospholipids (antiphospholipid antibodies) have been implicated in genesis of adverse pregnancy outcome, however, it has yet to be established that these antibodies are causative or that they are invariably associated with untoward perinatal outcome **(Lockwood et al., 1989)**.

EPH-Gestosis is one of most dangerous complications of pregnancy and is held responsible for a number of maternal mortality and morbidity **(Chamberlain et al., 1975)**. Some authors have noticed a relation between EPH-Gestosis and antiphospholipid antibodies **(Branch et al., 1989)**.

AIM OF THE WORK

The aim of this study is to detect the presence of antiphosphlipid antibodies (lupus anticoagulant and anticardiolipin antibodies) in cases of EPH-Gestosis.

Antibodies will be correlated with the severity of the disease and maternal complications of EPH-Gestosis.

I. ANTIPHOSPHOLIPID ANTIBODIES

(1) Introduction

(2) Diagnostic tests

(3) Prevalence

(4) Clinical association

(5) Pathognesis and mechanisms of actions.

1. INTRODUCTION

Antiphospholipid Antibodies (aPL):

In 1957 Laurell and Nilsson described a patient with five prior intrauterine fetal deaths who had a biologically false-positive test for syphilis and anticoagulant antibody. Later it was found that the circulating anticoagulant and the molecule resposible for the false positive serology was antiphospholipid antibodies.

These antiphospholipid antibodies are antibodies of any immunoglobulin type which can react with cardiolipin or any other negatively charged phospholipid in an enzyme-linked immunosorbant assay (ELISA) or radio immunoassay, which have lupus anticoagulant activity or which react in a serological test for syphilis. **(Koskia et al., 1989)**.

There are several antiphospholipid antibodies. The most relevant to the obstetrician are the lupus anticoagulant (LAC), the anticardiolipin antibody (ACA), and the antibody that causes false-positive syphilis test (BFP-St). The obstetric significance of antibodies against phosphatidylserine, phosphatidyl ethanolamine and phosphatidyle inositol is not yet clear.

I. Lupus Anticoagulant (LAC):

This was the name assigned by Feinstein and Rapaport (1972) to a factor causing inhibition of blood coagulation, which is immunoglobulin in

nature first described by Conley and Hartmann (1952).

These immunoglobulins are of IgM and IgG type which interfere with phospholipid dependant coagulation tests without inhibition of the activity of specific coagulation factors by binding to the Phospholipid portion of prothrombin-Prothrombinase complex (Xa, Va, phospholipid and ca). **(Harris et al., 1986)**. Fig. 1

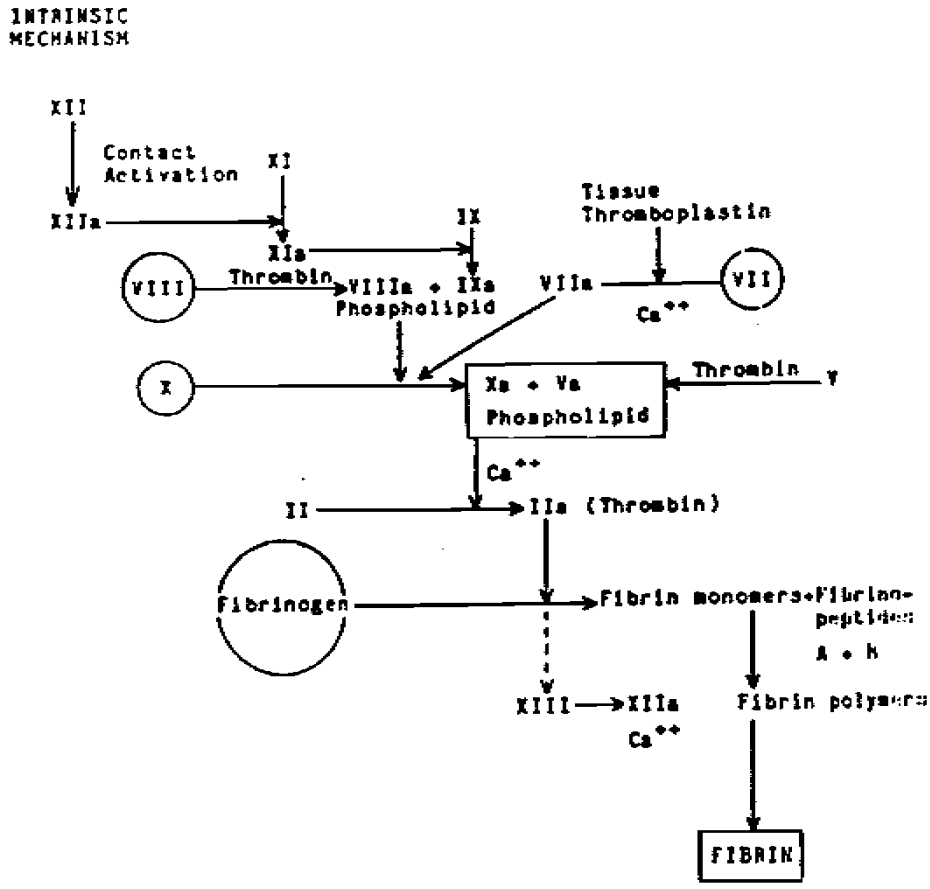


Fig. 1 (Harris et al., 1986).

So we can detect its presence in the plasma of the patients using this nature where it causes prolongation of activated partial thromboplastin time (A.P.T.T.) or other phospholipid dependant coagulation tests while they reflect conversion of prothrombin into thrombin using factor Xa.

Coagulation factor deficiency is excluded by retesting the sample after admixture with an equal volume of normal plasma, clotting time will not return to normal if the lupus anticoagulant is present. Sometimes the clotting time is further prolonged indicating a lupus cofactor which allows full expression of lupus anticoagulant activity.

There's a marked variability in many assays for LAC. **(Lesperance et al., 1988)**; **(Tripplet & Brandt., 1989)** among which the most sensitive assays are the kaolin clotting time, dilute russell's viper venom time & activated partial thromboplastin time using diluted thromboplastin. There's no agreement in the literature as to which of these tests is most sensitive or specific **(Machin et al., 1990)**. It's agreed that no single test can detect all L.A.C.

In contrast to the effect of LAC in vitro which cause prolongation of A.P.T.T, the prominent clinical association in vivo is with thrombosis **(Carreras and Vermylen., 1982)**.

It has proposed that LAC may produce local vascular thrombosis and infarction by inhibition of endothelial cells mediated Protien-C activation

which is a circulating inhibitor of several coagulation factors. **(Cariou et al., 1986)**.

Other mechanisms were suggested as a mode of action of LAC;

In vivo **Carreras and Vermylen 1982** found that LAC may bind to phospholipid in endothelial cell membrane and decreases prostacyclin production by blocking arachidonic acid release so the antagonist thromboxane will predominate and causes vasoconstriction followed by platelet aggregation and intravascular thrombosis. Also interferance with antithrombin III activity **(Casgriff and Martin, 1982)** or prekallekrin activity were postulated. Other mechanisms include platelet activation by the binding of L.A.C. to the membrane of platelets which contain phospholipids intiating aggregation and thrombosis.

LAC are not reported only in cases of SLE but it was found that about half of patients with antiphospholipid antibodies don't have SLE (primary antiphospholipid antibody syndrome) of these the minority have relatives with SLE or other collagen diseases.

In addition to the clinical association of these antibodies and other neurological syndromes such as multi infarcted dementia, white matter disease and demylinating myelopathies, it is associated also with thrombocytopenia, and vascular heart disease **(Alarcon Segoria & Sancky Guerrera., (1989), Harris et al., 1985)** and other autoimmune diseases in association with fetal losses in pregnancies, such as abortions or fetal deaths **(Branch et al., 1987)** especially in the second trimesters.

So the name lupus anticoagulant was derived from the fact that this antibody was found first in patient with lupus and acted as an anticoagulant by prolongation of the partial thromboplastin time (P.T.T). This name was a poor choice because soon it was found that LAC was present in many patients who did not have lupus and in the majority of patients the antibody was responsible for episodes of thrombosis rather than anticoagulation.

II. Anticardiolipin Antibodies (ACA):

Biochemistry of cardiolipin:

Cardiolipin is a very acidic negatively charged phospholipid composed of two molecules of phosphatic acid linked together through a molecule of glycerol. **(Thomas and Dovolein, 1982). Pangborn in (1947)** reported the occurance of a complex phosphatic acid compound in a beef heart and affixed the name cardiolipin to it. Apparently this compound represents an essential requirement for the complement binding activity of beef heart extracts with the sera of syphilitic subjects.

Later on Pangborn reported his observations on the chemical nature of the products of partial hydrolysis of cardiolipin as in Fig. 2

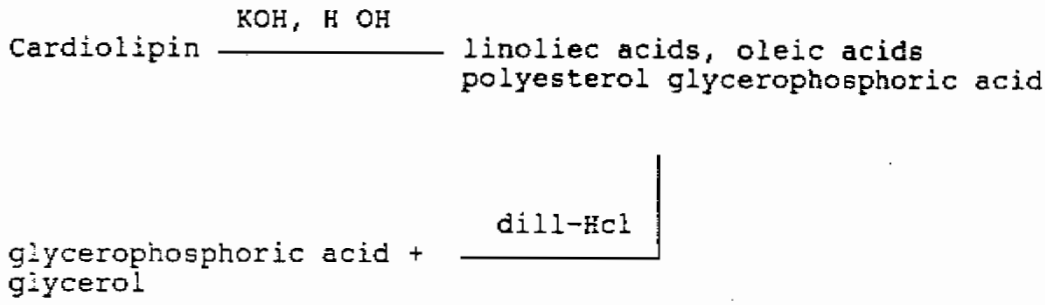
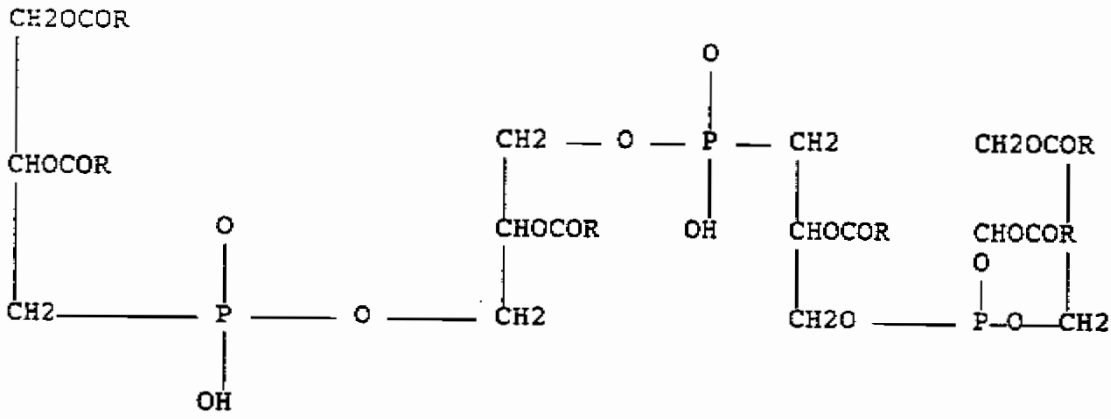


Fig. 2

On the basis of these observations, **Pangborn** proposed the following structure for this substance: Fig. 3



The Formula of cardiolipin as designated by pangborn (1947).

Fig. 3

Pangborn observed that the mixed fatty acids of cardiolipin were composed mainly of unsaturated fatty acids in the form of linoleic acid 72%, oleic acid 11%, linolenic acid 8% and palmitoleic acid 5.2%.