ANTICARDIOLIPIN ANTIBODIES
A CAUSE OF A TENDENCY TO THROMBOSIS

Thesis

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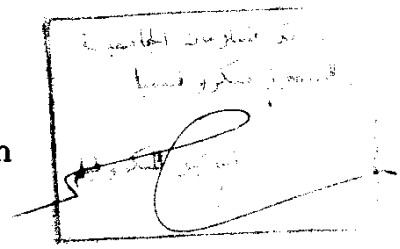

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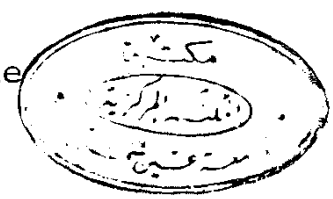

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بسم الله الرحمن الرحيم

وعلمك ما لم تكن تعلم وكان
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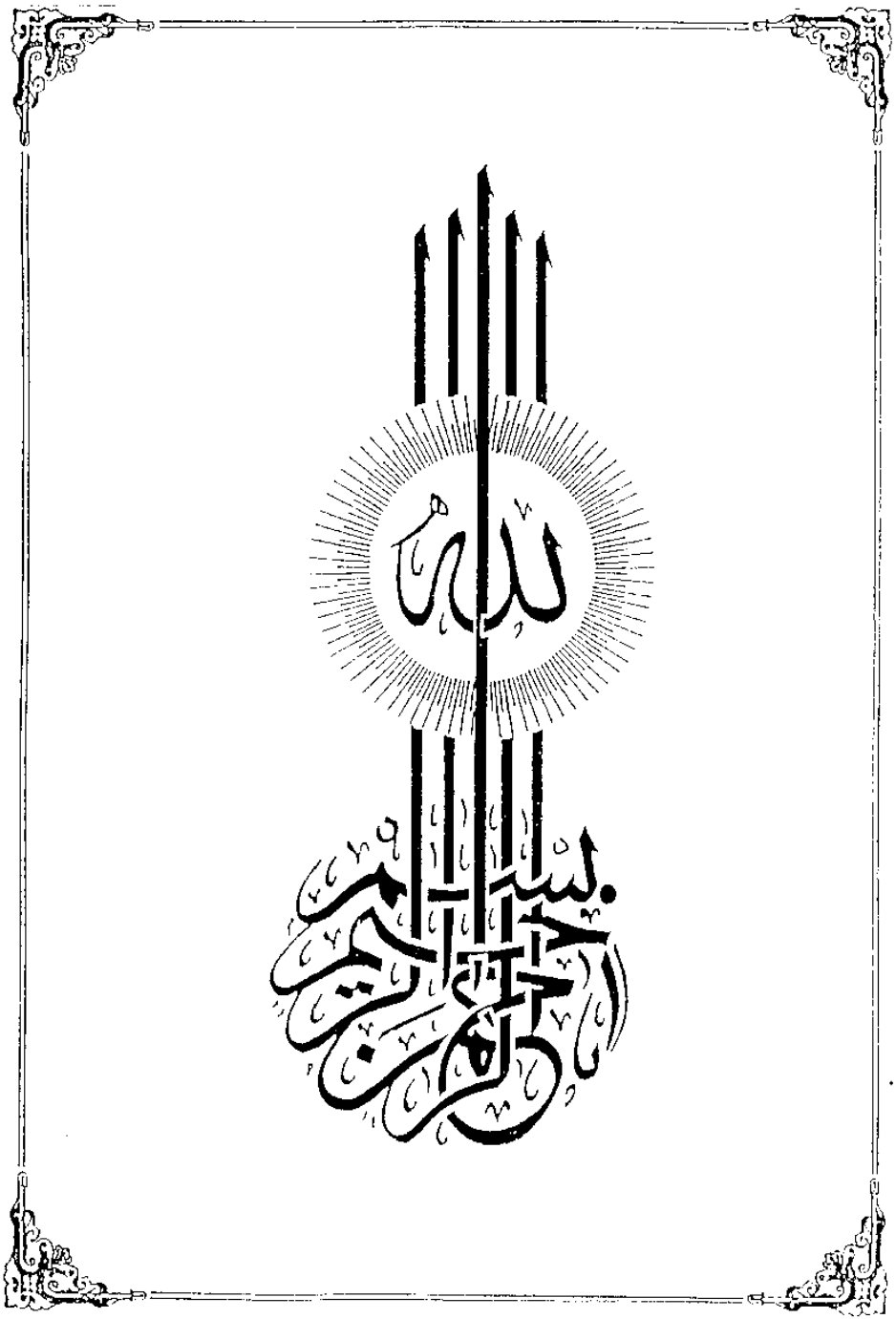

C O N T E N T S

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ABBREVIATIONS

aCL or ACLA or ACA	=	anticardiolipin antibody.
VDRL	=	Venereal Disease Reference (research) laboratory precipitation test.
S.L.E.	=	Systemic Lupus Erythematosus.
B.F.P.	=	Biological false positive reaction for syphilis.
A.P.T.T.	=	Activated partial thromboplastine time.
P.T.T.	=	Partial thromboplastin time.
anti-PL or APLA	=	antiphospholipid antibodies.
IgG, IgM, IgA	=	Immunoglobulin G, M, A.
L.A.C.	=	Lupus anticoagulant.
P.E.T.	=	Pre-eclamptic toxaemia.
H.L.A.	=	Human leucocytic antigen.
D.I.C.	=	Disseminated intravascular coagulopathy.
E.L.I.S.A.	=	Enzyme-linked immunosorbant assay.
E.E.	=	Ethinyl estradiol.

INTRODUCTION

I N T R O D U C T I O N

During the past few years a major and possibly common syndrome has been highlighted and its borders more clearly defined. The anticardiolipin syndrome consisting of a tendency to recurrent thrombosis, together with recurrent abortion, thrombocytopenia and neurological disease, is now known to be associated with antibodies against cardiolipin, while the original patients had lupus or its variants **(Harris E.N. et al., 1983).** It now appears that the association between thrombosis and antibodies against phospholipids such as cardiolipin may extend far beyond the confines of rheumatology **(Hughes et al., 1986).**

How important is the syndrome? What is its aetiological role in recurrent abortion, myocardial infarction, stroke and other thrombotic conditions?.

Is the tendency exacerbate by other factors such as contraceptive pill or smoking? What is the mechanism of thrombosis? When should patients be tested for the antibody and what should be done for those with high titres? The answer of these questions this syndrome has raised are not yet clearly defined **(Hughes and Khamashta, 1989).**

The present work will study the association between anticardiolipin antibodies and one of the thrombotic conditions: recurrent abortions aiming to evaluate the role of anticardiolipin antibodies in such condition. Also we will study the effect of taking contraceptive pill for a long period on the level of these antibodies. This work will be a trial to answer some of the question this syndrome has raised.

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REVIEW OF LITERATURE

CHAPTER I

ANTICARDIOLIPIN ANTIBODIES

Anticardiolipin antibodies are one group of the family of antibodies directed against negatively charged phospholipids. These include those responsible for a positive Venereal Disease Reference Laboratory precipitation test (VDRL) and for the lupus anticoagulant activity **(Harris E.N. et al., 1985 - Hamsten and Norberg, 1989).**

Anticardiolipin antibodies (ACL) are not a new discovery **(Laskin and Solonika, 1988).** They were probably first reported in 1904, when **Wasserman** described a complement fixation test to detect reagin in the sera of patients with syphilis. In **1941, Pangborn** showed that the antigen bound by reagin was an acid phospholipid obtained by alcohol extraction of ox heart muscle subsequently named cardiolipin.

Antiphospholipid antibodies are strongly associated with systemic and cerebral occlusive vascular disease in patients with S.L.E. and in those with lupus like disease and the primary phospholipid syndrome.

The first antiphospholipid syndrome to be described was the Biological False Positive (BFP) reaction for syphilis which appears to have no clinical association. The lupus anticoagulant is another APLA which often

occurs in association with the BFP **(Johansson E.A. & Lassus A. 1974)** and appears to have specificity for a range of phospholipids including cardiolipin **(Pengo et al., 1987).**

Some but not all of the patients with anticardiolipin antibodies have had demonstrable lupus anticoagulants and the titre of the anticardiolipin antibodies had been correlated with the degree of prolongation of the activated partial thromboplastin time (APTT) **(Harris E.N. et al., 1984).**

In a study done by **Harris et al., (1986)** suggest that patients with high ACA levels tend to have more than one of the clinical features associated with these antibodies namely thrombosis, fetal loss, thrombocytopenia and or a positive Coomb's test. This suggests that patients with high ACA levels who present with one clinical features such as thrombosis may develop other associated clinical features later in the course of their disease such as fetal loss or thrombocytopenia **(Harris et al., 1985).**

Most reports concentrate on systemic lupus erythematosus. Antiphospholipid antibodies have however, been described in a number of different conditions

including Sjogren's syndrome, systemic sclerosis **(Malia et al., 1988 and Shapiro, 1990)**, Rheumatoid arthritis **(Fort et al., 1987, Keane et al., 1987, Buchanan et al., 1989)**, Lyme disease **(Mackworth - Young et al., 1988)**, primary Sicca syndrome, dermatopolymyositis, psoriatic arthritis **(Russel R.C. et al., 1989, Buchanan et al., 1989)**, Behcet's syndrome **(Hull et al., 1984)**, syphilis **(Meyer et al., 1987)**, acute infections **(Vaarala et al., 1986)**, acquired immunodeficiency syndrome, infection with the human immunodeficiency virus HIV **(Canoso et al., 1987)**, infections mononucleosis, pneumocytis carinii pneumonia **(Masala et al., 1989)**, primary immunodeficiency diseases **(Pascual - Salcedo et al., 1988)**, and infective endocarditis **(Ashevson et al., 1990)**.

Some patients appear to have no underlying disorder, although there is an extremely low incidence of raised antiphospholipid antibodies in normal individuals **(Harris et al., 1985)**, some patients with an uncomplicated history of thrombosis or recurrent abortion have been shown to have raised antiphospholipid antibody levels. These individuals may be regarded as having a primary anti-phospholipid syndrome **(Mackworth - Young et al., 1989)**.

Anticardiolipin Ab in normal healthy individuals:

Many authors studied the prevalence of raised anticardiolipin antibody levels in normal healthy individuals. **Manoussakis et al., (1987)** detected raised aCL antibody levels in 2.3% of the 261 serum samples they had examined. Also, **Fields et al., (1989)** found that 2% of the 543 samples they had examined showed raised aCL antibody levels.

Anticardiolipin Ab in patients with systemic lupus erythematosus:

The average prevalence of raised anticardiolipin antibody level in SLE in the study done by **Love and Santoro (1990)** which was based on collecting data reported by other authers was 44%. No difference in the frequency of raised aCL antibody level was noted in patients taking cortiosteroids as compared with untreated patients **(Fort et al., 1987, Kalunian et al., 1988 and Love and Santoro, 1990).**

Raised anticardiolipin antibody level appeared not to correlate with age **(Fort et al., 1987, Shergy et al., 1988),** duration of the disease **(Kalunian et al., 1988 and Shergy et al., 1988)** or clinical manifestation of active disease (Neuropsychiatric manifestations

and thrombocytopenia were notable exceptions) **(Love and Santoro, 1990).**

Anticardiolipin Ab in patients with non-SLE disorders:

In recent years, there have been an increasing number of reports of antiphospholipid antibody in patients with non SLE disorders. Although the data base is still too small to support accurate estimates of prevalence in any one group, raised anticardiolipin antibody levels have been consistently associated with various autoimmune diseases and with certain drugs particularly those known to produce a lupus like - syndrome such as chlorpromazine, procainamide or hydralazine. It is also clear that the frequencies of antiphospholipid antibody raised levels in these conditions may approximate those seen in systemic lupus erythematosus **(Love and Santoro, 1990).**

Of special interest are the high frequencies of raised aCL antibody level reported in patients with non-autoimmune diseases such as infections and in elderly persons. The high prevalence of raised aCL antibody level in patients with non SLE disorders suggest that these patients make up a significant fraction of aCL positive population **(Love and Santoro, 1990).**