ANTIPHOSPHOLIPID ANTIBODIES IN VARIOUS DISEASE STATES

ESSAY

Submitted in Partial Fulfillment of the Master Degree in Clinical Pathology

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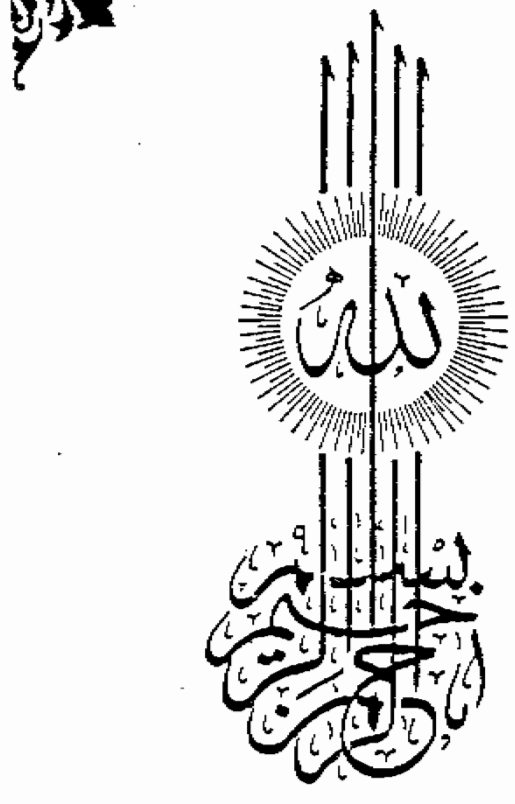

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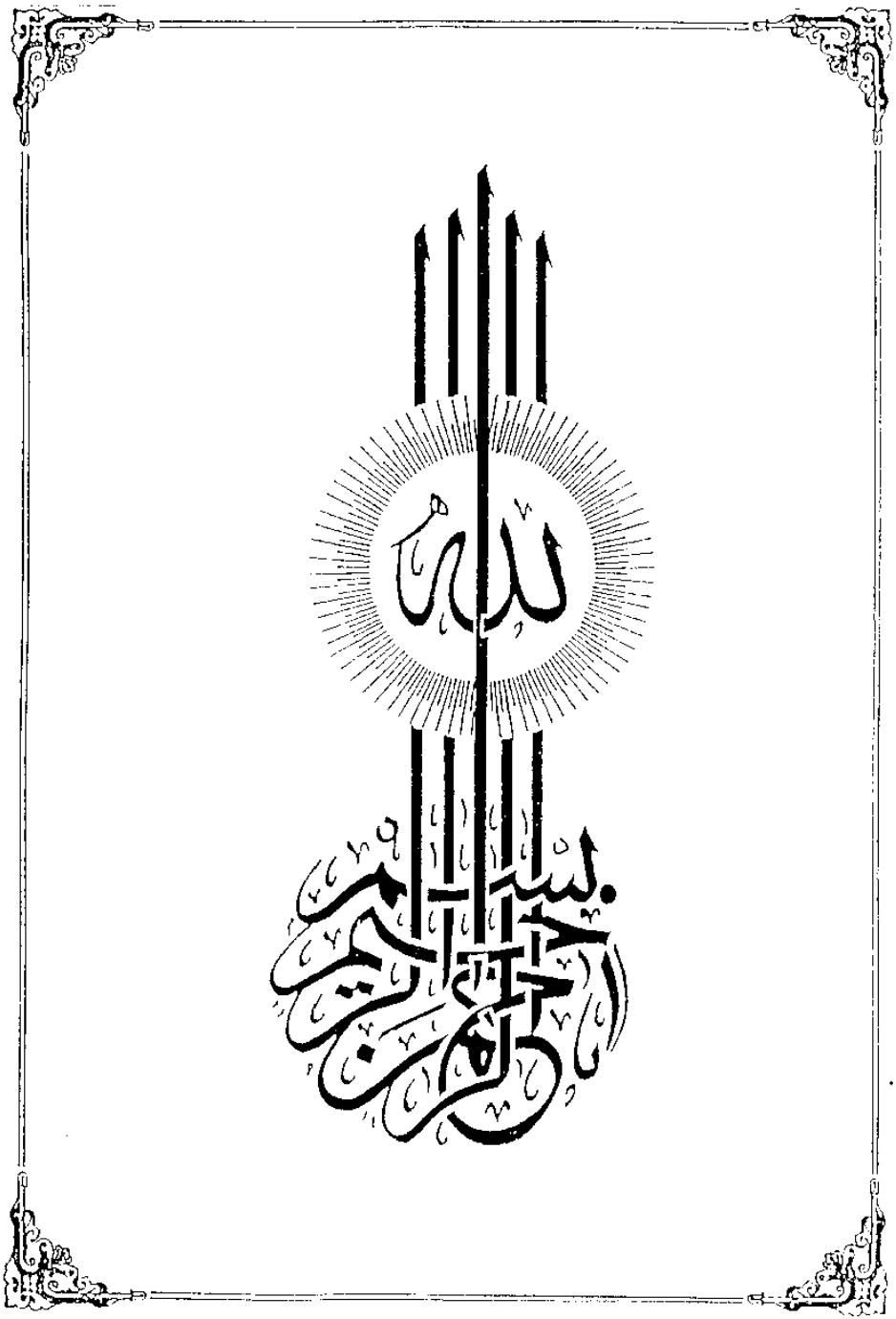

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LIST OF ABBREVIATION

aCL antibody	: Anticardiolipin antibody .
AMA	: Antimitochondrial antibody .
aPL antibody	: Antiphospholipid antibody .
apTT	: Activated partial thromboplastin.
BFP-STS	: Biological false positive serological test of Syphilis .
Ca ++	: Calcium .
CHOL	: Cholesterol .
CL	: Cardiolipin .
CNS	: Central nervous system .
dKCT	: delta kaolin clotting time .
dRVVT	: dilute Russell Viper Venom time .
ds DNA	: double stranded DNA .
ELISA	: Enzyme linked immunosorbent assay.
HIV	: Human immune deficiency virus.
LA	: Lupus anticoagulant .
LE cell	: Lupus erythematosus cell.
M Nacl	: Molar sodium chloride.
M NaI	: Molar sodium iodide .
PA	: Phosphatidic acid .
PAI-1	: Type 1 plasminogen activator inhibitor.
PAPS	: Primary antiphospholipid syndrome.
PC	: Phosphatidyl choline .

PE	: Phosphatidyl ethanolamine .
PG	: Phosphatidyl glycerol.
PI	: Phosphatidyl inositol.
PS	: Phosphatidyl serine .
PT	: Prothrombin Time .
RA	: Rheumatoid arthritis .
SLE	: Systemic lupus erythematosus.
SM	: Sphingomyelins .
T4	: T helper lymphocyte.
T8	: T suppressor lymphocyte .
T-PA	: Tissue type plasminogen activator.
TTI	: Tissue thromboplastin inhibition test.
VDRL	: Venereal disease research laboratory antigen.

INTRODUCTION AND AIM OF THE WORK

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Antiphospholipid antibodies are a group of auto-antibodies , mainly IgG and IgM class , directed predominantly , against negatively charged phospholipids. Several recent studies have found that patients with these antibodies are prone to repeated episodes of venous and arterial thrombosis , recurrent fetal loss , and thrombo-cytopenia.

In addition , there have been reports of the possible association of antiphospholipid antibodies with heart valve lesions , hemolytic anemia , and neurological events such as cerebrovascular accidents and chorea , patients with these clinical and serological features have been defined as having the antiphospholipid syndrome .

Our study aims to find in which circumstances should these antibodies be sought and which laboratory test is the best to detect them .

REVIEW OF LITERATURE

HISTORICAL BACKGROUND OF ANTIPHOSPHOLIPID ANTIBODIES

The study of antiphospholipid (aPL) antibodies began in 1907 when Wasserman introduced a diagnostic test for syphilis using a saline extract of liver from fetuses with congenital syphilis as the antigen to detect an antibody reagin in the sera of patients with syphilis (Mc Neil et al., 1991).

In 1938 , a program of premarital and antepartum mass blood screening for syphilis was instituted in the United States and extended to military personnel during world warII. As a result, it became clear that there were a large number of people with positive tests for syphilis without clinical or epidemiological evidence of the disease . This phenomenon was referred to as the biological false positive serological test for syphilis (BEP-STS). This was noted in two situations first, reagin was detected in the serum of patients during or after a number of infections with no syphilis, disappeared following recovery from the infection and was known as the acute BFP-STS. The second type, known as the chronic BFP-STS, there was absence of precipitating factors and it persisted over many months or years (MC Neil et al.,1991).

In 1941 ,Pangborn demonstrated that the active antigenic component was a phospholipid , which she termed cardiolipin (CL), and subsequently all tests had in common the principle of detection of antibodies to extracted CL (Harris , 1990) .

During the 1950 s, Moor and his colleagues studied a cohort of chronic BFP-STS reactors and noted a high incidence of autoimmune diseases . Systemic lupus erythematosus (SLE) was found particularly or developed in the ensuing years of observation (Mc Neil et al.,1991).

In 1952 , Conley and Hartmann described a unique coagulation inhibitor in two patients with SLE who had BFP-STS reactions , whose plasma demonstrated prolongation of in vitro coagulation and also demonstrated a prolongation of the whole blood clotting time . In 1955, Frick described a similar inhibitor in an individual who did not have SLE , but also had a BFP-STS . This was the first demonstration that this inhibitor can occur independently of SLE (Vermylen , 1986) .

The term lupus anticoagulant (LA) was firstly introduced in 1972 by Feinstein and Rapaport , who also found that this LA prolonged the whole blood clotting time and occasionally the prothrombin time, but no specific deficiency of any clotting factors was detectable (Feinstein and Rapaport, 1972).

The association between LA and BFP-STS was increasingly recognized, but of interest is the fact that the LA is not found in patients with syphilis (Johansson and Lassus , 1974) . Numerous studies on the mechanism of action

of LA were performed by Breckenridge et al. in 1963 and by Lechner in 1974 , they agreed that LA interferes with interaction of performed prothrombin activator complex with prothrombin . Also there was evidence that LA is an immunoglobulin directed against the phospholipid portion of the prothrombin activator complex (Shapiro and Thiagarajan,1982).

Lechner (1974) and Shapiro and Thiagarajan (1982) fractionated LA positive plasma and found the nature of the LA and its inhibitory effect on in vitro clotting, it became clear that most patients possessing LA do not suffer haemorrhagic complications even during surgery .

As early as 1963, Bowie and co-workers found four out of eight patients with LA who had suffered thromboembolic phenomena (Vermylen,1986). Later on , it was observed that if bleeding occurs it is almost always due to prothrombin deficiency or thrombocytopenia , and occurs rarely in association with LA alone (Feinstein and Rapaport,1972). This was confirmed in Lechner's review (Lechner, 1974), who also noted a high incidence of BFP-STS, thrombosis, and thrombocytopenia in patients with LA compared to those without.

The LA , is not specific for SLE as it has been described in healthy individuals, other autoimmune diseases , and in association with certain drugs , infections and malignancies (Derksen and Kater , 1985) .

CHEMISTRY AND PHYSICAL PROPERTIES OF PHOSPHOLIPIDS

Phospholipids are lipids containing , in addition to fatty acid and an alcohol , a phosphoric acid residue .They are composed of a glycerol backbone with a phosphodiester group at C3 linked to a polar head group alcohol ,and two esterified fatty acid chains at C1 , and C2 (Harper etal.,1977) .

Naturally occurring phospholipids contain saturated fatty acids at C1 locus , but those at C2 position are usually unsaturated (Merill and Nichols, 1985) .
Phospholipids derive their names from the head group alcohol . In human cells , these head groups consist of either a nitrogenous base choline, ethanolamine, serine , glycerol, inositol or sphingosine . The resulting phospholipids are :

1- Phosphatidic acid and phosphatidyl glycerol ,
2- Phosphatidyl choline,
3- Phosphatidyl ethanolamine,
4- Phosphatidyl inositol,
5- Phosphatidyl serine,
6- Lysophospholipids,
7- Plasmogens and
8- Sphingomyelins . (Harper et al., 1977).