AUTOANTIBODIES AS A DIAGNOSTIC TOOL

Essey

submitted for partial fulfilment of
Master Degree in Clinical and Chemical Pathology

By

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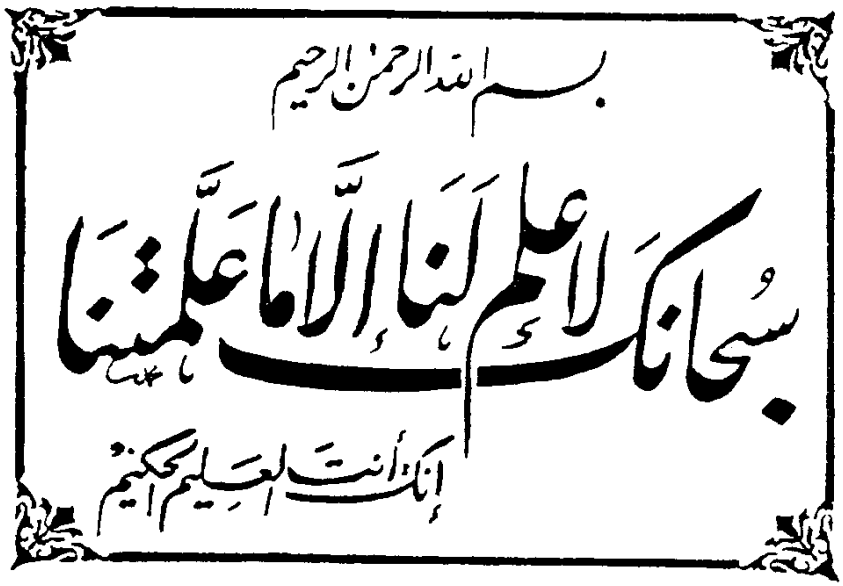

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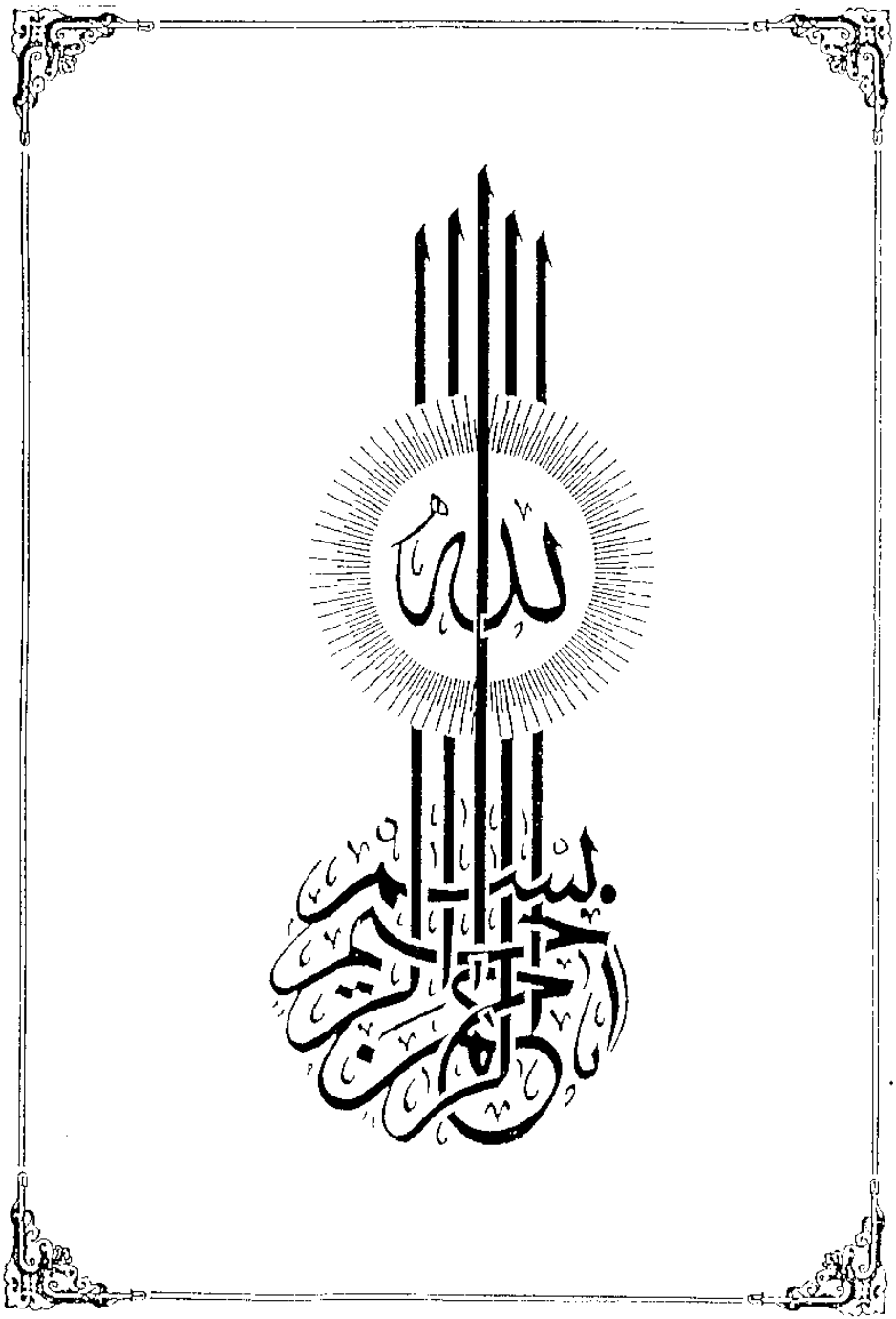

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LIST OF ABBREVIATIONS

Ach R	: Acetyl choline receptors.
Acl	: Anticardiolipin.
AMA	: Anti-mitochondrial antibodies.
ANA	: Anti-nuclear antibodies.
APS	: Anti-phospholipid syndrome.
AST	: Aspartate transaminase.
ASGP-R	: Asialoglycoprotein receptor.
BCOADC	: Branched chain 2-oxoacid dehydrogenase complex.
CA2	: Second colloid antigen.
CAH	: Chronic active hepatitis.
cAMP	: Cyclic adenosine monophosphate.
CIE	: Counter immunoelectrophoresis.
CL	: Crithidia luciliae.
DM	: Dermatomyositis.
DNA	: Deoxyribonucleic acid.
ds-DNA	: Double stranded deoxyribonucleic acid.
Elisa	: Enzyme linked immunsorbant assay.
ENA	: Extractable nuclear antigen.
FAb	: Fragment antigen binding.
FANA	: Fluorescence anti-nuclear antibody test.
FC	: Fragment crystallizable.
G-C	: guanine-cytosine.
HBs Ag	: Hepatitis B surface antigen.
HIV	: Human immunodeficiency virus.
HLA	: Human leucocyte antigen.

HPM : Hepatocyte plasma membrane.

IAA : Insulin autoantibodies.

ICA : Islet cell antibodies.

ID : Immuno-diffusion.

IDDM : Insulin dependent diabetes mellitus.

IgG : Immunoglobalin G.

IgM : Immunoglobalin M.

JRA : Juvenile rheumatoid arthritis.

LATS : Long acting thyroid stimulator.

LKM : Liver and Kidney microsomal antibodies.

LSP : Liver specific protein.

MCTD : Mixed connective tissue disease.

M2 : Trypin sensitive inner mitochondrial membrane.

MG : Myasthenia gravis.

MIR : Major Immunodominant region.

NOMA : Naturally occuring mitochondrial antibodies.

OGDC : Oxoglutarate dehydrogenase complex.

PCNA : Proliferating cell nuclear antigen.

PBC : Primary biliary cirrhosis.

PDC : Pyruvate dehydrogenase complex.

PEG : Polyethylene glycol.

PM : Polymyositis.

PSC : Primary sclerosing cholangitis.

RA : Rheumatoid arthritis.

RANA : Rheumatoid arthritis associated nuclear antigen.

RF : Rheumatoid factor.

RIA : Radioimmunoassay.

RNP : Ribonucleoprotein.

Ros : Reactive oxygen species.

RTE : Rabbit thymus extract.

SD : Sarcosine dehydrogenase

SDS-PAGE: Sodium dodecyl sulphate polycrylamide gel electrophoresis.

SLA : Soluble liver antigen.

SLE : Systemic lupus erythematosus.

SMA : Smooth muscle antibodies.

SM : Smith antigen.

SMP : Submitochondrial particle.

SS : Systemic sclerosis.

SS-A/Ro : Sjogren's syndrome antigen A.

SS-B/La : Sjogren's syndrome antigen B.

SS-DNA : Single stranded deoxyribonucleic acid.

Str-Ab : Striational autoantibodies.

Tg : Thyroglobulin.

Tpo : Thyroid peroxidase.

TsAb : Thyroid stimulating antibody.

TSH : Thyroid slimulating hormone.

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Introduction and Aim of The Work

INTRODUCTION

Autoantibodies are antibodies capable of reacting with self components.

Grabar (1975) was of the opinion that autoantibodies have a biological function to act as "transporting" agents for cellular breakdown products, thereby, aiding their disposal. This may be true, however, what is more important is the autoimmune phenomenon which appear in relation to certain defined human diseases.

Serum autoantibodies frequently produce valuable diagnostic markers for such diseases. Of these ANA and anti-DNA and their value in the diagnosis of SLE is well known.

At the same time, autoantibodies have a prognostic value and are of value in screening for people at risk, e.g., relatives of patients with autoimmune diseases.

AIM OF THE WORK

The aim of this study is to review precisely the role of autoantibodies as a diagnostic and prognostic tools for many autoimmune diseases.

Review of Literature

AUTOANTIBODIES

Garbar (1975) proposed that autoantibodies were preserved throughout evolution because they have a physiologic role. He suggested that autoantibodies are "transporteurs" or carriers of metabolic and catabolic tissue degradation products, and function as cleansing agents that eliminate waste products from the organism (Roitt, 1977 and Parker, 1980). The transient appearance of autoantibodies after burns and myocardial damage would illustrate this (Mandel et al., 1977).

Although there is little evidence to support this theory, the concept that autoantibodies might be physiologic deserves consideration (Parker, 1980). In clinical medicine, there are numerous examples of autoantibody production without autoimmune disease, certain infectious disorders tending to chronicity, many drugs and the process of aging are associated with a limited form of autoimmunity. Upon successful eradication of the infection or discontinuation of the offending drug the manifestations of autoimmunity disappear. The infectious agents or drugs may induce cell membrane changes that are recognized immunologically. For example, procainamide is a drug that can induce a lupus-like syndrome. The development of lupus is associated with the appearance of antilymphocyte antibodies, suggesting possible

interaction of procainamide with the lymphocyte membrane (Bluestein et al., 1979).

AUTOIMMUNITY:

Autoimmunity defines a state in which the natural unresponsiveness or tolerance to self terminates. As a result, antibodies or cells react with self constituents, thereby causing disease (Theofilopoulos et al., 1987).

The primary etiology of autoimmune diseases is still obscure. It has been postulated that a normal immunological mechanism may be stimulated by an abnormal stimulus to develop an immune reaction against the body's own tissue such an abnormal stimulus may arise from the release of a normally sequestrated antigen by inflammation or tissue injury into the circulation where it comes in contact with immunocompetent cells. It is recognized as foreign and elicits an autoimmune response. Examples of such sequestrated autoantigens are thyroglobulin, spermatozoa and lens proteins. There is little evidence today for the antigen sequestration theory, for example, a normal individual have antigen-binding lymphocytes with specificity for thyroglobulin (Grabar, 1975).

An individual becomes tolerant or unresponsive to his own tissue antigens during early development of the immune system as a result of direct contact between self tissue