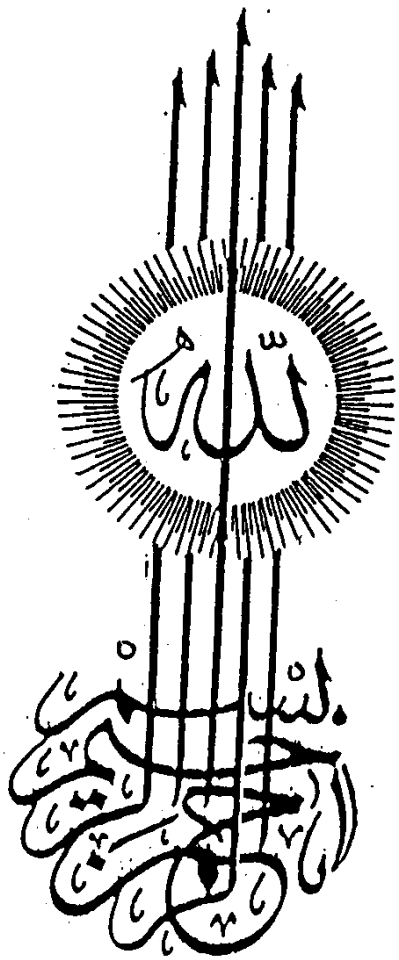


RECENT IMMUNOLOGICAL ASPECTS AND MANAGEMENT OF CHRONIC IDIOPATHIC THROMBOCYTOPENIC PURPURA IN INFANCY AND CHILDHOOD

ESSAY

Submitted in Partial Fulfilment of M.Sc. Degree in Paediatrics

BY

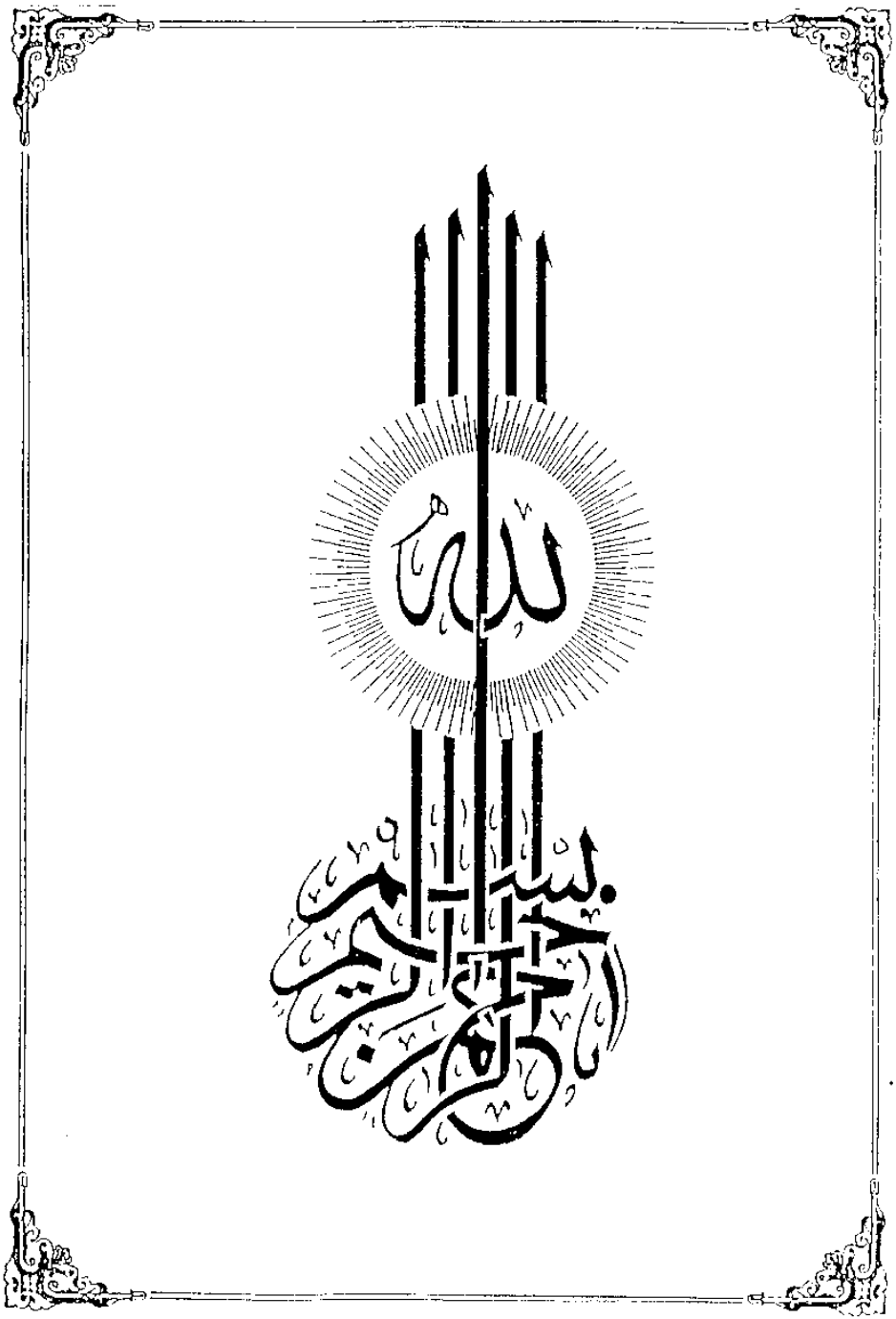
HASSAN ALI HAFEZ EL-HAFEZ
(M.B., B.Ch.)

SUPERVISED BY

Prof. Dr. OMAR HELMI
Professor of Paediatrics
Head of Paediatric Department
Faculty of Medicine
Ain Shams University

FACULTY OF MEDICINE
AIN SHAMS UNIVERSITY

1986



TO MY PEOPLE

ACKNOWLEDGEMENTS

I wish to express my cordial appreciation to Prof. Dr. Omar Helmi, Professor of Paediatrics and Head of Paediatric Department - Ain Shams University, for his unfailing guidance, supervision and kind encouragement throughout this piece of work.

I am also indebted to Dr. Sanaa Abd-el-Rahman, Assistant Lecturer of Paediatrics - Ain Shams University, for her kind help all through the preparation of this essay.

CONTENTS

LIST OF ABBREVIATIONS

Å	Angstrom
C	Complement
dl	decilitre
fg	femtogram
HLA	Human Leucocyte Antigen
Ia	Immune response region - associated antigen
ITP	Idiopathic Thrombocytopenic Purpura
kg	kilogram
uCi	microcurie
ug	microgram
mg	milligram
MHC	Major Histocompatibility Complex
ul	microlitre
ml	millilitre
mmol	millimole
min	minute
S	Svedberg
SCCS	Surface Connected Canalicular System

INTRODUCTION

INTRODUCTION

Idiopathic thrombocytopenic purpura (Werlhof's disease, purpura haemorrhagica, essential thrombocytopenia, autoimmune thrombocytopenia) has been the subject of an everexpanding work, studying its pathogenesis, diagnosis and management.

The immunologic basis of this disease is coming more and more under focus, especially through the advent of monoclonal and anti-idiotype antibodies, as invaluable research tools that have revolutionized immunology.

There are two, quite different, syndromes included under the term idiopathic thrombocytopenic purpura (ITP) : the acute and the chronic forms. The former is mainly preceeded by infection whereas the latter is not. The antibodies mediating the platelet

in either type, are distinct; also the antigens to which these antibodies are directed, are quite different. In the paediatric age-group, the acute form predominates below the age of 10 years, whilst the chronic form is commoner in those above the age of 10 years, especially in females.

AIM OF THE ESSAY

AIM OF THE ESSAY

The aim of our essay is to highlight recent immunologic aspects concerning the pathogenesis, diagnosis and treatment of chronic idiopathic thrombocytopenic purpura, in infancy and childhood. Special emphasis will be made in reviewing pathogenesis and treatment.

REVIEW

Platelet structure and function

Blood platelets in the quiescent state, are small, anucleate discoid cells, much like miniature versions of discuses thrown by athletes. In human blood, the platelets normally number 130 000 - 400 000/ul, have an average diametre of 2 - 3 microns, and an average volume of 8 cubic microns. The outside cell surface is generally smooth, with occasional pockmarked indentations where channels of the " Surface Connected Canalicular System (SCCS) " exist (Nichols et al, 1984). Within the cell, organelles - including dense granules, alpha granules, lysosomes, peroxisomes and mitochondria - are randomly seen. Also scattered throughout the cell cytoplasm are glycogen granules. In the plane of largest diametre, a bundle of microtubules curves around below the cell membrane, encircling the cell. The SCCS connects the interior of the platelet to the exterior. The second tubular system within the platelet is the dense tubular system, a smooth endoplasmic reticulum, closely associated with the SCCS, and with the circumferential microtubule band. Contractile proteins are present in the cytoplasm. Resting platelets do not adhere to one another, nor to endothelial surfaces (Gerrard & Friesen, 1985).

The platelet may also be regarded as being composed of 3 zones : the peripheral zone, the sol-gel zone, and the organelle zone. The peripheral zone, in turn, is formed of 3 parts: an exterior coat, a unit membrane, and a submembrane area. The exterior coat is 150 - 200 Å thick, and shows no firm evidence of precise arrangement. In it is present protein antigens, highly specific glycoproteins, several enzymes, and also comprises adsorbed plasma proteins. The unit membrane is a

typical trilaminar plasmamembrane, and it supplies lipid activator to coagulation. The submembrane layer contains fine filaments that may help support the discoid shape of the platelet - at rest - and the pseudopodia formed after activation. The second zone is the sol-gel zone (hyaloplasm), which in turn is composed of 3 parts: an annular bundle of filaments around the greatest circumference - the SCCS - 250 Å in thickness. The second system of fibres is 50 Å thick, and the third is submembranous filaments. The third zone is the organelle zone, which contains granules, dense bodies and mitochondria (White, 1983).

In the circulation, platelets normally travel separately, showing little tendency to interact with each other, or with the endothelial cells that form the capillaries and line the walls of larger blood vessels. When injury occurs, however, the platelets are suddenly brought into contact with collagen, a ubiquitous tissue component from which platelets are usually kept apart by the thin vascular endothelium. This contact with collagen initiates an integrated series of events, the final outcome of which is the formation of a haemostatic plug, composed of thousands of platelets fused into a single mass.

The encounter of a platelet with a collagen fibril provokes major changes in the platelet's shape and properties. A disc at rest, the collagen-stimulated platelet rapidly assumes the shape of a sphere. Its granules retreat to the centre, and from its surface sprout a number of long, thin, spine-like projections known as filipoda. The platelet becomes very sticky, attaching tightly to the exposed collagen fibril in a process known as adhesion. It then undergoes the " release reaction ", a complicated series of events during which the alpha- and the