PLATELET AGGREGATION IN CHRONIC LIVER DISEASES

THESIS

Submitted for Partial Fulfilment
for
MASTER DEGREE
in
CLINICAL PATHOLOGY

BY
YASSER FOUAD M. THABET

UNDER SUPERVISION OF

Prof. Dr. OSAIMA EL SAYID SELIM
Prof. of Clinical Pathology
Faculty of Medicine
Ain Shams University

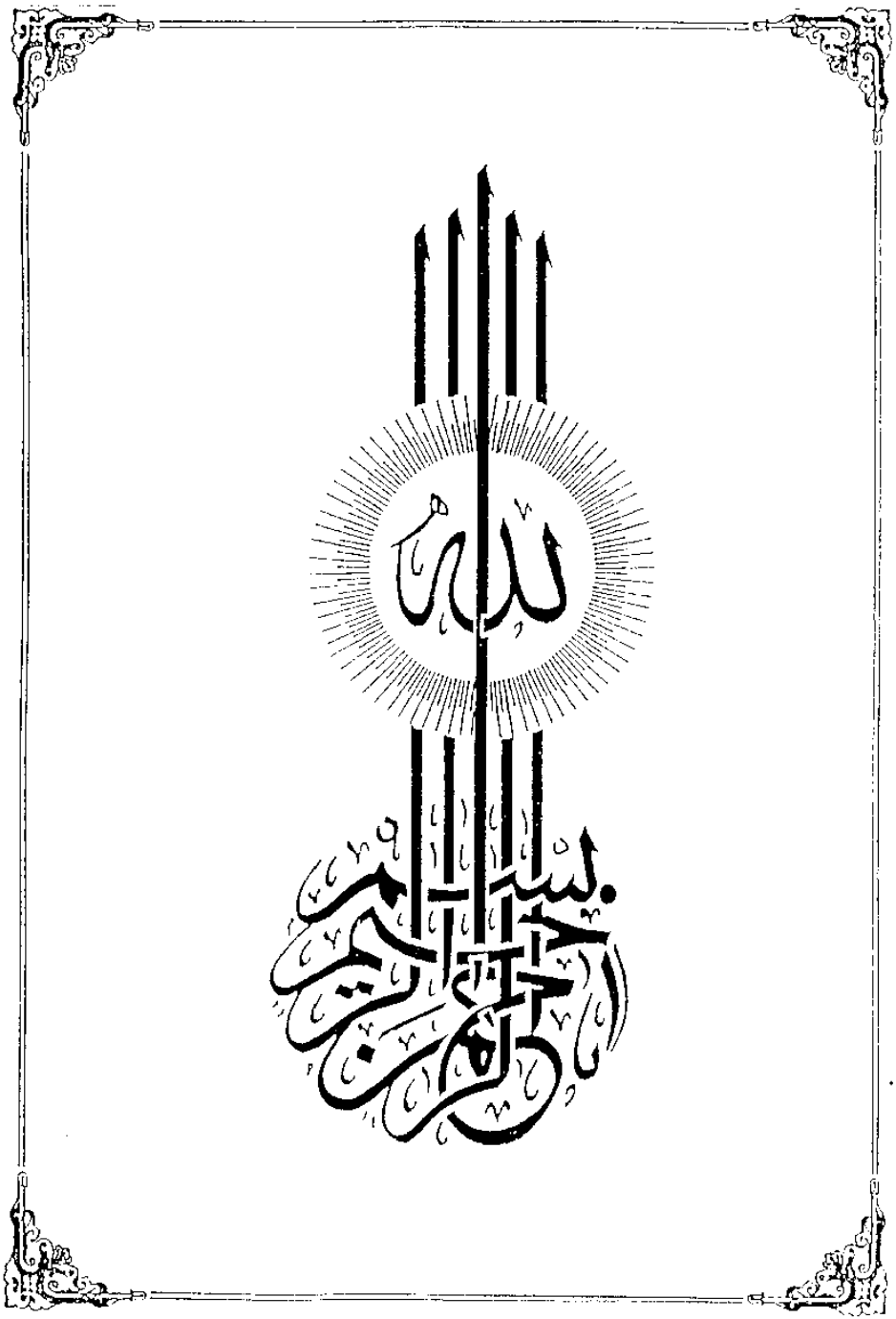
Prof. Dr. ABD EL-RAHMAN EL-ZAYADI
Prof. of Tropical Medicine
Facultyof Medicine
Ain Shams University

Dr. ZEINAB TAWFIK
Assistant Prof of Clinical Pathology
Faculty of Medicine
Ain Shams University

1987

إعداد الدكتور / سلوى يوسف
أستاذ مساعد الباثولوجيا الإكلينيكية

دياس ثابت



ACKNOWLEDGEMENT

I would like to express my deep gratitude to Prof.Dr. OSAIMA EL SAYID SELIM Professor of Clinical Pathology, Ain Shams University for her great help and valuable direction. Her suggestions and precious advices are deeply appreciated.

I am very grateful to Prof. Dr. ABD EL RAHMAN EL-ZAYADI Professor of tropical medicine, Ain Shams University who helped me to overcome all the clinical problems and continuously guiding me to the essential points for sucess of this work.

I would like to thank Dr.ZEINAB TAWFIK Assistant Prof of Clinical pathology, Ain Shams University who offered all facilities to acheive the practical part of this thesis. Her advices was of great benefit.

Also, I would like to thank Dr. FADYA ABO BASHA Director of Bolood Transfusion Center, Ain Shams Specialized Hospital for her great helpful to complete this work.

My sincere thanks to the staff of clinical pathology department, and endoscopic units in Ain Shams University Hospital for their kind help and facilities they offered me.

The Candidate

CONTENTS

		Page
ABBREVIATIONS		1
INTRODUCTION		2
CHAPTER ONE:	PLATELET ANATOMY	3
CHAPTHER TWO:	PLATELET PHYSIOLOGY AND FUNCTION	10
CHAPTER THREE:	THE FIBRINOLYTIC SYSTEM	21
CHAPTER FOUR:	CHRONIC LIVER DISEASES	27
CHAPTER FIVE:	MATERIALS AND METHODS	33
CHAPTER SIX:	RESULTS	48
CHAPTER SEVEN:	DISCUSSION	63
CHAPTER EIGHT:	SUMMARY AND CONCLUSION	70
CHAPTER NINE:	REFERENCES	74
CHAPTER TEN:	ARABIC SUMMARY	

REVIEW OF LITERATURE

ABBREVIATIONS

ABBREVIATIONS

ADP	Adenosine diphosphate.
ATP	Adenosine triphosphate.
BT	Bleeding time.
CAH	Chronic active hepatitis.
FDP's	Fibrin/fibrinogen degradation products.
PC	Platelet count.
PPP	Platelet poor plasma.
PRP	Platelet rich plasma.
PT	Prothrombin time.
PTT	Partial thromboplastin time.
SCT	Staphylococcus clumping test.

INTRODUCTION

INTRODUCTION

Haemorrhagic disorders are common in patients with chronic liver diseases which are endemic in Egypt due to bilharziasis and viral hepatitis.

Current concepts of hemostasis emphasize the central role of platelets in the formation of a hemostatic plug.

Interferance with normal platelet function therefore is particularly a main cause for hemostatic disterbance in patients with chronic liver diseases.

Fibrinogen / fibrin degradation products have been demonstrated in the blood of cirrhotic patients, and such products when formed in vitro, can interfere with normal platelet aggregation.

This work aims to throw light on platelet aggregation and try-to quantify its real importance in relation to various haemorrhagic phenomena in cases of chronic liver diseases at the same time try to find other changes in haemostasis that may lead to bleeding tendencies in these patients.

CHAPTER ONE

PLATELET ANATOMY

CHAPTER ONE

PLATELET ANATOMY

History:

In the early part of the nineteenth century, many investigators observed the blood platelets but even Zimmermann, 1860, Maxschultz, 1865 and Osler 1874 who realized that these particles are not artifacts but failed to recognize their true importance.

Morphology:

The platelets in peripheral blood are heterogenous with respect to size, density and staining characteristics. Their morphology varies greatly depending on the methods by which they are examined, the anticoagulant used and temperature.

They circulates as variable sized disc shaped bodies of 3.6 ± 0.7 um in diameter, 0.9 ± 0.3 um in thickness and 70.0 ± 4.8 fl in volume with mean surface area of 22.2 um^3 (Frojmovie, 1976).

On Romanovsky stained peripheral blood smears, platelets are small formed elements and usually contain purplish granules, while by electron microscopic studies, their surface is found to be irregular and contain indentation which are thought to represent the opening of an elaborate system of

tubules which extends through the interior of platelets (Hoving , 1968). Under dark field illumination, they are translucent and have a sharp contour with few immobile granules in the center of the cells (Maupin, 1969).

Ultra Structure of Platelets:

With electron microscope, platelet can be divided into several different regions including: peripheral zone, sol gel zone, organelle zone (White 1981) and membrane system (Vermylen et al., 1983).

I. Peripheral Zone:

It is composed of a double layer of phospholipid in which are embeded glycolipids, cholesterol and protein. Some phospholipids are negatively charged and are distributed primarily on the inner layer of the membrane. Some evidences suggest that these negatively charged phospholipids move to the outer layer of the membrane when platelets are activated.

The exterior coat extends 150-200 A° from the phospholipid layer. It is composed of several elements including carbohydrate-rich protein, glycolipids, mucopolysaccarides and plasma protein which are adsorbed on to the platelet surface.

This membrane mediates the platelet's interaction with its environment and occupies a central position in platelet physiology.

II. Sol Gel Zone:

This is composed of the platelet's cytoskeleton which maintains the resting disc shap, the explosive shape changes and in which the organelles are embedded. This zone includes:

(A) Contractile Proteins:

Actin is the most abundant platelet protein, represents 20% of the total platelet protein. It is a mixture of two single chain protein of molecular weight 44,000 that are similar to but not identical with muscle actin.

Myosin is composed of 6 polypeptide chains and although it is analogous to skeletal muscle myosin, it is immunologically different. All the six chains are contractile to the dimeric head region (Booyse and Rafelson, 1971).

(B) Platelet Microtubules:

Composed of two major proteins of 55,000 molecular weight in association with several high molecular weight protein called tubulin (White , 1968). This is a ring like structure which

may be only a single microtubule surrounding the platelet several times before terminating into two free ends.

(C) The Microfilaments:

It is about 50A° in diameter. They are essential for contractile mechanism of platelets.

Both microfilaments and microtubules make waves of contraction during the discharge of platelet contents after stimulation.

III. The Organelle Zone:

Platelets contain a large number of organelles and particulate elements which are embedded in the sol gel matrix with random distribution and become centralized upon activation. This includes platelet granules, dense bodies, mitochondria and golgi apparatus.

(A) Granules:

They can be divided into α -granules, lysosomes and peroxisames (Bentfeld and Barker, 1982). The α -granules are the most numerous and contain a large number of proteins which can be released from platelets when they are stimulated. Platelet granules contents are mentioned in Table No. (1).