STUDY OF FIBRINOGEN AND FIBRINOLYTIC ACTIVITIES IN LEUKEAMIA AND MALIGNANT LYMPHOMAS.

THESIS

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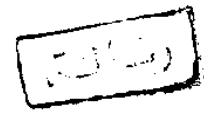

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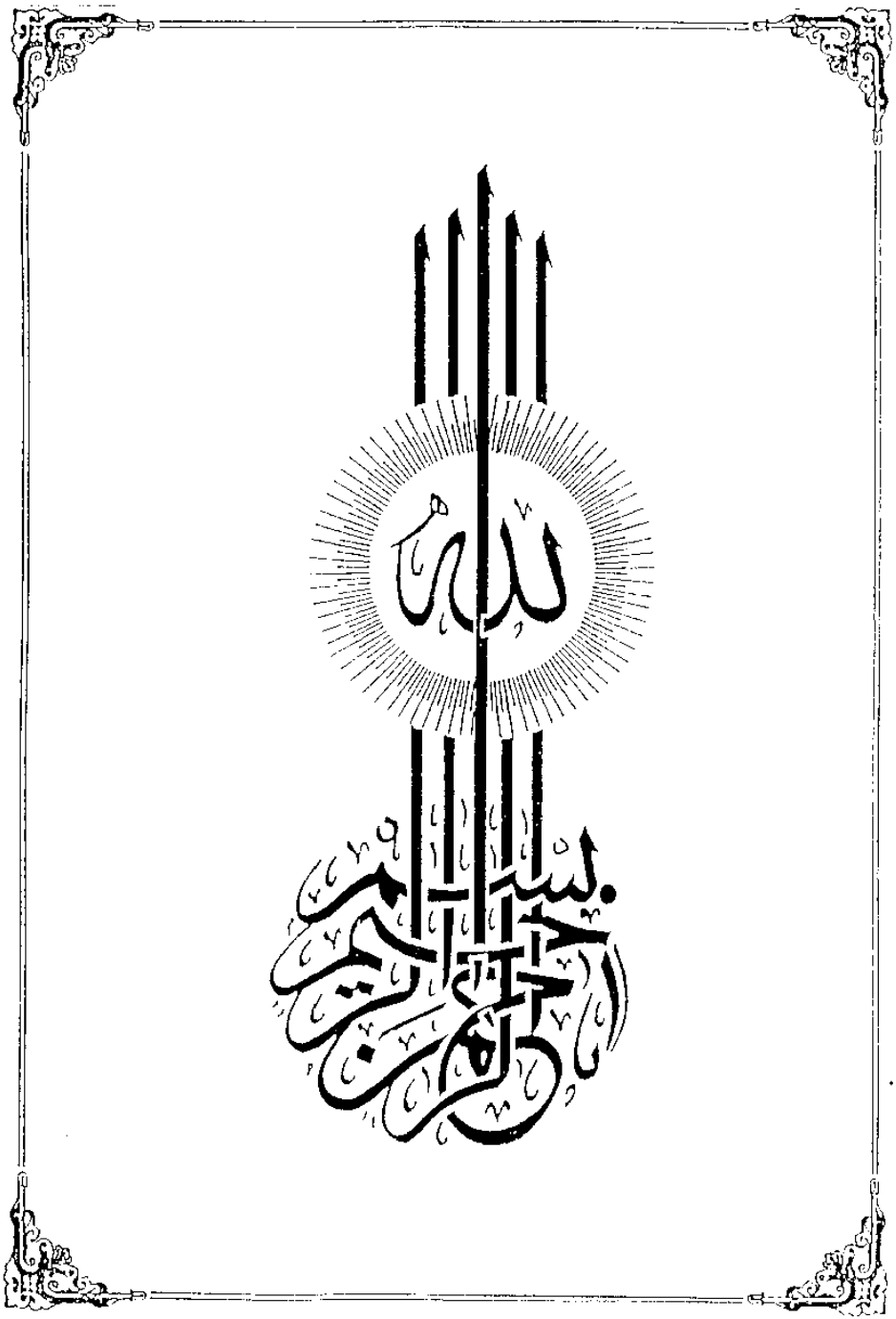

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LIST OF ABBREVIATIONS

ACTH	:	Adreno Cortico Trophic Hormone.
AMCA	:	Amino Methyl Cyclohexane Carboxylic Acid or Tranexamic acid.
AL	:	Acute Leukeamia .
CLL	:	Chronic Lymphocytic Leukeamia.
CML	:	Chronic Myelocytic Leukeamia.
DIC	:	Disseminated Intravascular Coagulation.
EACA	:	Epsilon Amino Caproic Acid .
EDTA	:	Ethylen Diamine Tetraacetic Acid.
ELT	:	Euglobulin Lysis Time.
FDP	:	Fibrin(gen) Degradation Products.
FSF	:	Fibrin Stabilizing Factor.
Hb	:	Haemoglobin .
HUS	:	Haemolytic Ureamic Syndrome.
$M \pm$ S.D.	:	Mean $\pm$ Standard Deviation
MES	:	2N Morpholine Ethan-Sulphonic Acid.
ML	:	Malignant Lymphomas.
MM	:	Mixed Moulds.
MP	:	Mixed Pollens.
NH_4-C_2 H_4	:	Ammonium Oxalate Powder.
PF-3	:	Platelet Factor-3
PPP	:	Platelet Poor Plasma.

PRP	:	Platelet Rich Plasma
RBC'S	:	Red Blood Corpuscles.
Sec	:	Seconds
SF	:	Step Phenomenan.
STT	:	Serial Thrombin Time.
TTP	:	Thrombotic Thrombocytopenic Purpura.

C O N T E N T S

AIM OF THE WORK

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Along the course of different haemopoietic malignancies, there is, at a time, certain degree of blood loss. The blood loss in such cases has different forms and variable severity. Blood loss may be the presenting symptom in many cases with malignant blood disorders . Moreover, some of these cases are discovered accidentally during the search for a systemic or specific cause of serious haemorrhage, e.g. vitrious or brain haemorrhages(Wintrobe, 1968).

Many abnormalities in the hemostatic mechanism were accused in the pathogenesis of haemorrhage in malignant haemopoietic disorders. Since, thrombocytopenia is rather a constant finding in most of malignant haemopoietic disorders, it was incriminated as the basic cause of haemorrhagic tendencies in such cases(Pisciotta & Schultz,1955).

Yet, it was found that the magnitude of thrombocytopenia in many cases is not sufficient alone to give clinical bleeding. It was then suggested that the coagulation mechanism may be disordered in one or more of its steps. Several reports are available about decrease in the plasma activity of factor V,VII and prothrombin(Gilbert & Wasserman, 1964). Again ,

these descrete abnormalities in the coagulation mechanism are not sufficient to induce haemorrhage. By the advent of interest in the platelet function rather count abnormalities, it was found that malignant haemopoietic disorders may accompanied by defective platelet function such as: impaired adhesion and aggregation or defective release reaction, "thrombocytopathia". (Lewis, 1957).

The position of fibrinolytic disorders among the different aetiologic factors inducing bleeding is not yet fully elucidated in many disease states. It is considered that fibrinolytic hyperfunction may be a factor which can precipitate, modify or prolong the bleeding when other factors are grossly affected.Thus, in haemophilia which is well known as a haemorrhagic tendency due to heriditary deficiency of factor VIII (antihaemophilic globulin), the fibrinolytic mechanism intruded as a subsidiary factor, while when hyperfunctioning, may precipitate or prolong an attach of bleeding in a haemophiliac. Antifibrinolytic agents(e.g. Epsilone Amino Caproic Acid) are now used in haemophiliacs during attacks of bleeding(McNicol and Douglas,1972). The consideration of fibrinolytic hyperfunction in haemophilia has solved the amazing observation, why we may have two

haemophiliacs with similar plasma factor VIII activities, one of them is bleeding and the other is not ?

As regards the malignant haemopoietic disorders, the same situation may be present and we may have a group of patients with nearly similar platelet count and function and similar coagulation mechanisms, yet, some of them are bleeders and some are not.

The study of fibrinolytic mechanism in these patients is worthly so as to localize actual participation in the causation of haemorrhage. The aim of this work is to study the fibrinolytic mechanism in patients with malignant haemopoietic disordersto elucidate properly the defects in this system which might be of importance in the prognosis and management of patients .

REVIEW OF LITERATURE

CHAPTER I

REVIEW OF LITERATURE

1.1. Fibrinogen

Fibrinogen is one of the least soluble and larger proteins in the plasma (Wintrobe, 1967). Its molecular weight is 330,000. It is a glycoprotein composed of three pairs of polypeptide chains and has a basic role in the heamostatic mechanism (Blomback,1969;Mckee et al.,1970).

Fibrinogen is the precursor of the clot-forming protein fibrin. It is essential for the formation of blood clots (Wintrobe, 1967). The end result of conversion of fibrinogen to fibrin during blood coagulation is the formation of a fine network of fibres which entangles the cellular elements of the blood and forms the blood clot. Clotting of fibrinogen and the stabilization of the clot depend on the functions of two proteins , thrombin and the fibrin stabilizing factor(factor XIII) (Sjouquist 1959; Sherry et al., 1964; Iorand, 1965 ; Blomback et al., 1966).

Thrombin :

Is a hydrolytic enzyme which hydrolyses four specific arginyl-glycine bonds of each fibrinogen molecule, and two pairs of fibrino-peptides are released(Bailey and Bettelheim, 1955).