# OUTCOME OF HEMOSTASIS IN CORONARY HEART DISEASES AND THEIR CORRELATION WITH RISK FACTORS

## THESIS

Submitted for partial fullfilment of
M.D. Degree in **Clinical and Chemical Pathology**


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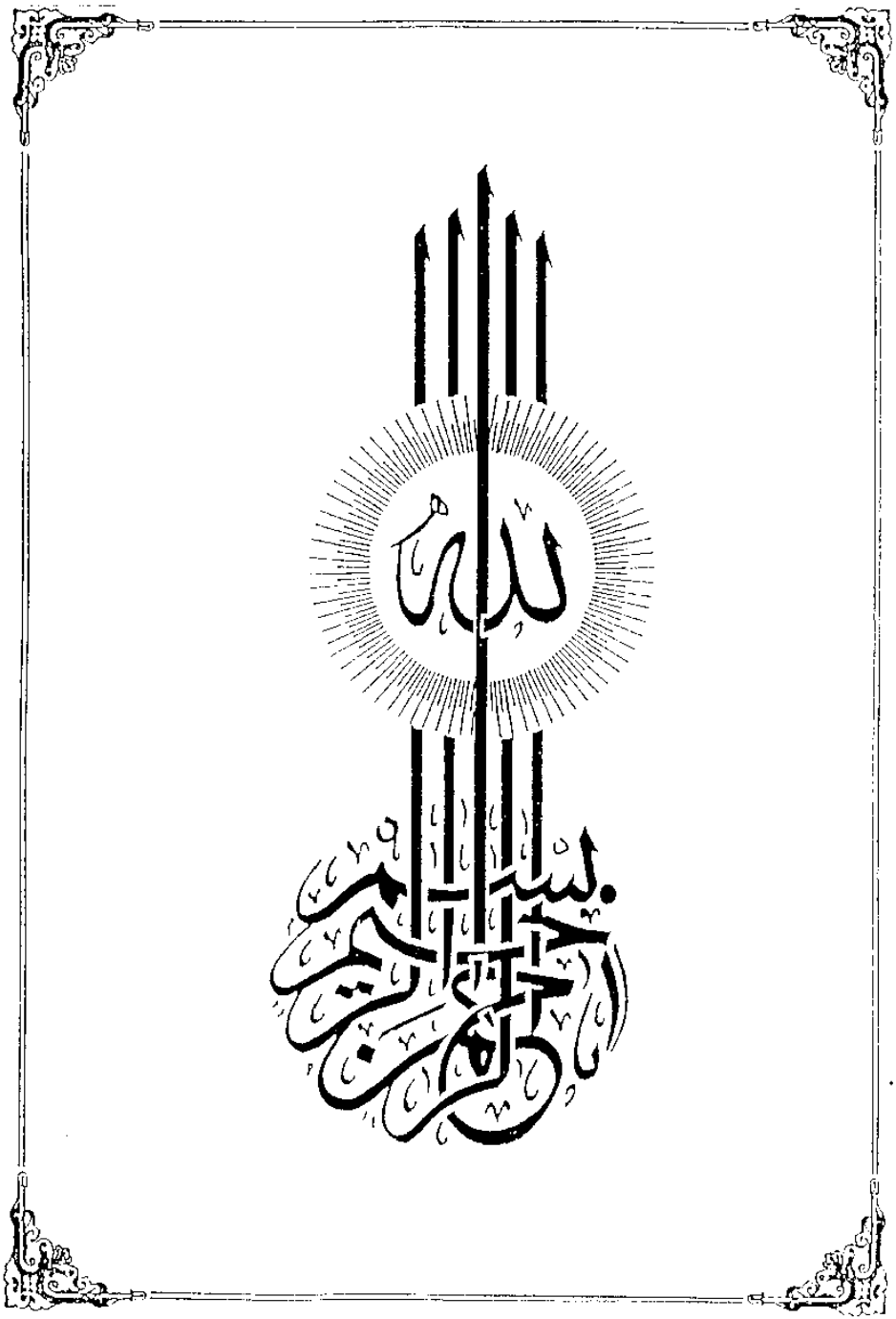
**FACULTY OF MEDICINE**
**AIN SHAMS UNIVERSITY**
**1992**



To My Parents;

Who suffered too much
and received too little.

## ACKNOWLEDGMENT

I wish to express my deepest gratitude to **Professor Dr. Nehayet Mahmoud Azmy, Professor of Clinical Pathology, Ain Shams University**, for her continuous help, advise and encouragement. In spite of her overcrowded time, she offered me a great help and valuable discussion that attended every stage in this work.

I am also deeply indebted to **Professor Dr. Tarik Hamza Salam, Professor of Clinical Pathology, Ain Shams University**, for his valuable suggestions and wise guidance that contributed to the success of the present work. His extreme patience and untiring effort are more than I can express.

I would also like to express my deep appreciation to **Professor Dr. Zeinab Tawfik, Professor of Clinical Pathology, Ain Shams University**, for her supervision and support.

I have also received unforgettable assistance and helpful instruction from **Dr. Salwa Aboul-Hana, Assistant Professor of Clinical Pathology, Ain Shams University**. I wish to express my deep gratitude to her.

I am grateful to **Dr. Samir Saleh Wafa, Lecturer of Cardiology, Ain Shams University**. He offered me all the cases included in this study.

I gratefully appreciate the valuable help of **Dr. Aza Sadek, Lecturer of Clinical Pathology, Ain Shams University**, for her unlimited help.

Finally, my deepest thanks to **my family and my colleagues** for their good help received in many ways.

# LIST OF ABBREVIATIONS

| | |
|---|---|
| ADP: | ADENOSINE DIPHOSPHATE |
| AMI: | ACUTE MYOCARDIAL INFARCTION |
| AMP: | ADENOSINE MONOPHOSPHATE |
| APO-B: | APOLIPOPROTEIN-B |
| aPTT: | ACTIVATED PARTIAL THROMBOPLASTIN TIME. |
| AT-III: | ANTITHROMBIN-III |
| CAD: | CORONARY ARTERY DISEASE. |
| CFU-E: | COLONY FORMING UNITE-ERYTHROCYTE. |
| CFU-Mg: | COLONY FORMING UNITE-MEGAKARYOCYTE. |
| CM: | PLATELET SURFACE MEMBRANE. |
| DB: | DENSE BODY |
| DIC: | DISSEMINATED INTRAVASCULAR COAGULOPATHY. |
| DTS: | DENSE TUBULAR SYSTEM. |
| EC: | EXTERIOR COAT. |
| ELT: | EUGLOBULIN CLOT LYSIS TIME. |
| FV: | FACTOR-V. |
| FVa: | ACTIVATED FACTOR-V. |
| F-VIII-vWF: | FACTOR-VIII-von-WILLEBRAND FACTOR. |
| FDPs.: | FIBRIN OR FIBRINOGEN DEGRADATION PRODUCTS. |
| 5-HT: | 5-HYDROXY TRYPTAMINE. |
| FPA: | FIBRINOPEPTIDE-A. |
| G: | ALPHA GRANULES. |
| Gla: | GAMMA-CARBOXYLATED GLUTAMIC ACID. |
| Gly: | GLYCOGEN |
| GMP: | GUANIDINE MONOPHOSPHATE |
| GP: | GLYCOPROTEIN. |
| Hb: | HEMOGLOBIN. |
| HDL: | HIGH DENSITY LIPOPROTEIN. |
| HMWK: | HIGH MOLECULAR WEIGHT KININOGEN. |
| HMWKa: | ACTIVATED HIGH MOLECULAR WEIGHT KININOGEN. |
| IHD: | ISCHEMIC HEART DISEASE. |
| IL-3: | INTERLEUKIN-3. |
| LDL: | LOW DENSITY LIPOPROTEIN. |
| M: | MITOCHONDRIA |
| MT: | MICROTUBULES. |
| NSAID: | NON-STEROIDAL ANTI-INFLAMMATORY DRUGS. |
| OCS: | OPEN CANALICULAR SYSTEM. |
| PA: | PLASMINOGEN ACTIVATOR. |
| PAF: | PLATELET ACTIVATING FACTOR |
| PAI-I: | PLASMINOGEN ACTIVATOR INHIBITOR-1. |
| PDGF: | PLATELET DERIVED GROWTH FACTOR. |
| PF-4: | PLATELET FACTOR-4. |
| $PGI_2$: | PROSTAGLANDIN $I_2$. |
| PNL: | POLYMORPHONUCLEAR LEUCOCYTES. |
| PROTEIN Ca: | ACTIVATED PROTEIN-C |
| PT: | PROTHROMBIN TIME |

| | |
|---|---|
| SFMC: | SOLUBLE FIBRIN MONOMER COMPLEXES |
| SMF: | SUBMEMBRANOUS FILAMENT |
| t-PA: | TISSUE PLASMINOGEN ACTIVATOR. |
| TT: | THROMBIN TIME |
| VLDL: | VERY LOW DENSITY LIPOPROTEIN |
| vWF: | von-WILLEBRAND FACTOR |
| WBCs: | WHITE BLOOD CELLS. |

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# Introduction And Aim Of Work

Most workers who are interested in thrombotic lesions of the heart accept that, atherogenesis and thrombogenesis are the two elements of great importance in the etiology of coronary heart disease *(Smith and Ashall, 1985)*.

So far, most of epidemiological and etiological researches on ischemic heart diseases have mainly dealt with conventional risk factors such as atherogenesis, but studies on hemostatic system have been insufficient to clarify the problem *(Sagrue et al., 1985)*.

Detailed investigations have demonstrated occlusive thrombi in coronary arteries in 95% of cases with acute localized infarction and 74% of cases with sudden cardiac death *(Davis and Thromas, 1984)*. Thus, the end point is a thrombotic episode, but no hemostatic factors were investigated in most of the major epidemiological or intervention trials.

After thrombosis or recurrent thrombotic episodes, there is no single test that detects the thrombotic tendency. However, the study of the activity and count of platelets, detection of consumption or increased activity of coagulation factors, thrombin activation and fibrinolysis point to the possible mechanism for thrombotic tendency. Besides, the other risk factors such as diet,

smoking, stress or family history of thromboembolism which are clearly relevant *(Lowe et al., 1981)*.

The last fragment of hemostasis is the very important part of hemostatic pathway. It has a decisive role in the outcome of hemostatic responses. Thrombin activation and fibrinolytic mechanism are good representative for this part of hemostasis.

The symptoms and signs of ischaemia in patients with coronary heart diseases could be related to a hypercoagulable state. Such a condition might be detected by elevated fibrinogen level *(Yarnell et al., 1985)*.

Fibrinopeptide A is the first peptide released from fibrinogen by thrombin to produce fibrin I. The half life of fibrinopeptide A in vivo is calculated to be 3 minutes and its measurement in blood can serve as an in vivo index of intravascular thrombin action *(Nossel, 1976)*.

## *AIM OF THE WORK:*

The aim of this work is to assess the thrombotic activation and fibrinolytic mechanism in patient with coronary diseases in a trial to find correlation between the hemostatic activity and risk factors.

# Review of Literature

# I. HEMOSTASIS

Hemostasis is the combined effect of various mechanisms involved in the prevention of spontaneous hemorrhage and in the arrest of escape of blood from the injured vessels.

The mechanism of hemostasis comprises the function of four components: vessel wall, platelets, coagulation system and fibrinolytic system. All components must be functioning correctly if hemostasis is to be normal *(Fig. 1,2)*.

**Vascular System:**

The normal vascular morphology is comprised of three discrete layers, the intima, the media, and the adventitia. The intima is a continuous monolayer of non-thrombogenic endothelial cells that rests on subendothelium secreted by the cells. Media is formed of smooth muscles. Adventitia is comprised of an external elastic lamina and supportive connective tissue *(Stemerman, 1982)*.

*A. The role of vascular endothelium in hemostasis:*

The vascular endothelium is important to prevent oozing of blood from circulation. The vascular endothelium contains contractile protein fibers, i.e., stress fibres. These fibres are

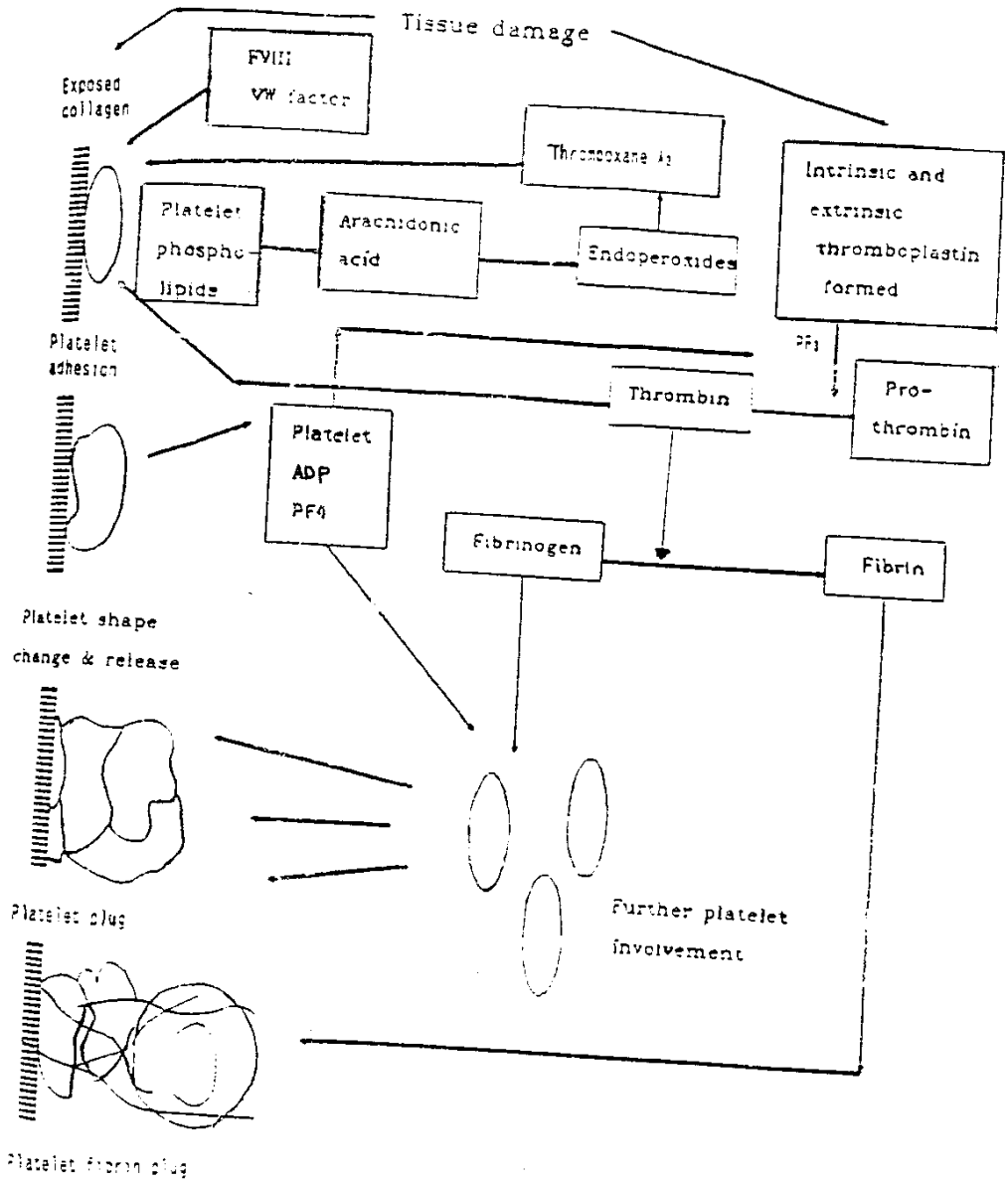


*FIG. (1): INTERACTION BETWEEN PLATELETS, PLASMA FACTORS AND VESSEL WALL IN HEMOSTASIS*

$PF_3$ = PLATELET FACTOR-3