# A REVIEW ON HAEMOSTASIS IN LIVER DISEASES

ESSAY

SUBMITTED FOR PARTIAL FULFILMENT

FOR THE MASTER DEGREE IN CLINICAL

PATHOLOGY.

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بسم الله الرحمن الرحيم

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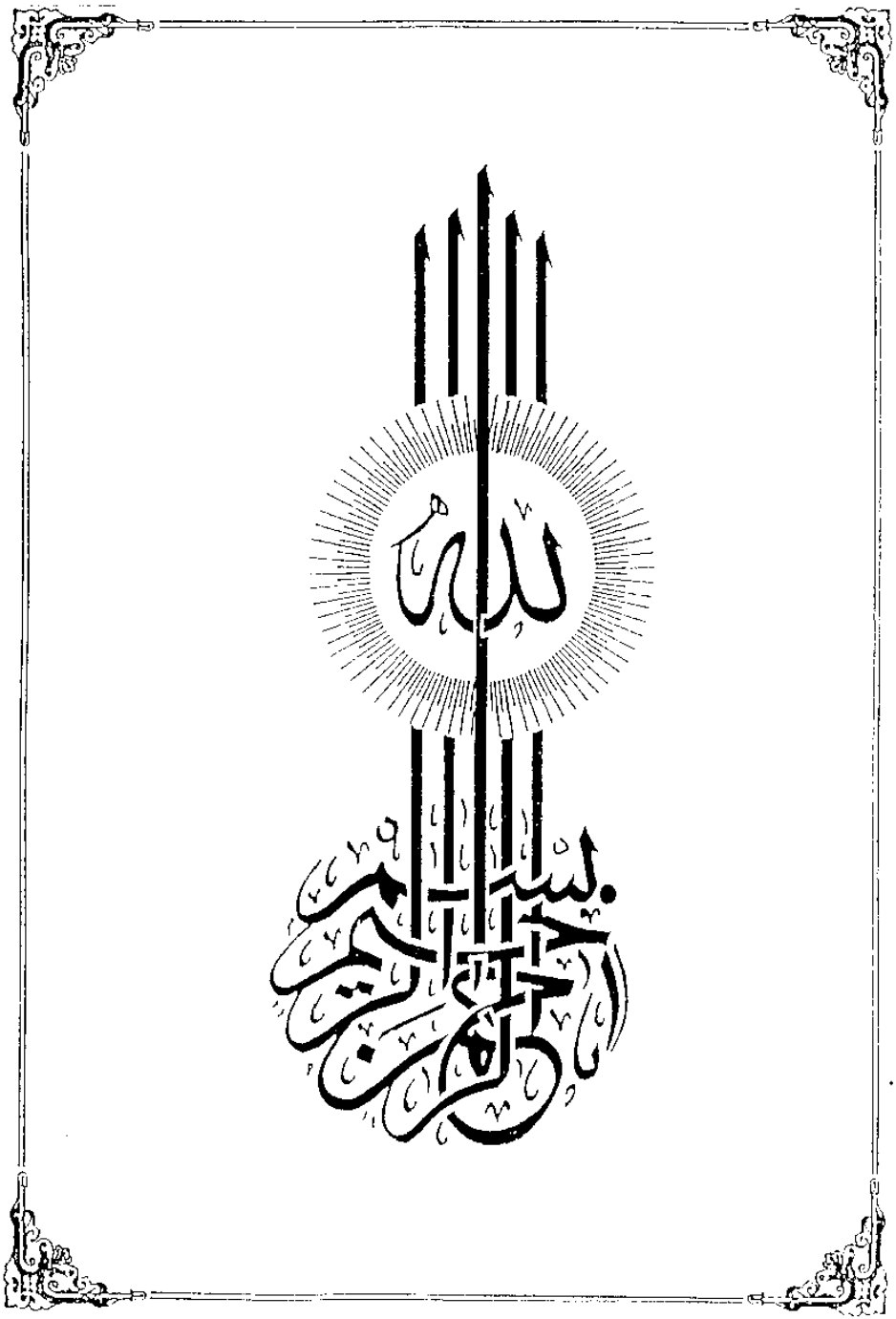
صدق الله العظيم



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# ABBREVIATION

| | | | |
|---|---|---|---|
| 1 | ADP | : | adenosine diphosphate |
| 2 | ATP | : | adenosine triphosphate |
| 3 | AT III | : | anti thrombin III |
| 4 | AAT | : | alpha 1 - antitrypsin |
| 5 | $Ca^{++}$ | : | calcium ions |
| 6 | DIC | : | disseminated intravascular coagulopathy |
| 7 | F.D.P.s | : | fibrin degradation products |
| 8 | HMWK | : | high molecular weight kininogen |
| 9 | PDGF | : | platelet derived growth factor |
| 10 | $PGI_2$ | : | prostacyclin |
| 11 | $^{75}Se$ | : | selenomethionine |
| 12 | VIII:vWF: | | von Willebrand factor |

# Introduction

# INTRODUCTION

## Haemostasis:

The normal haemostatic mechanism is a complex process which prevents blood loss from intact vessels and arrest bleeding from injured vessels. It consists of two main components, the haemostatic system and the inhibitory system (Coombs, 1984).

Haemostasis is normally mediated by the combination of three processess: the contraction of the blood vessels, the adhesion and aggregation of platelets and the process of blood or plasma coagulation. Despite their physiologic importance, the process of platelet aggregation and blood coagulation may constitute a threat to the body if they propagate beyond the wound site. This is controlled by fibrinolysis and natural inhibitors of coagulation (Penner, 1980).

Liver disease, is a frequent cause of haemostatic abnormalities which may be associated with clinically significant haemorrhage. The pathogenesis of the

haemostatic disorder is complex and includes decreased synthesis of haemostatic factors, synthesis of structurally abnormal factors, disseminated intravascular coagulation, thrombocytopenia, failure of hepatic clearance mechanisms and the abnormalities of fibrinolysis. (Borzovic, 1982).

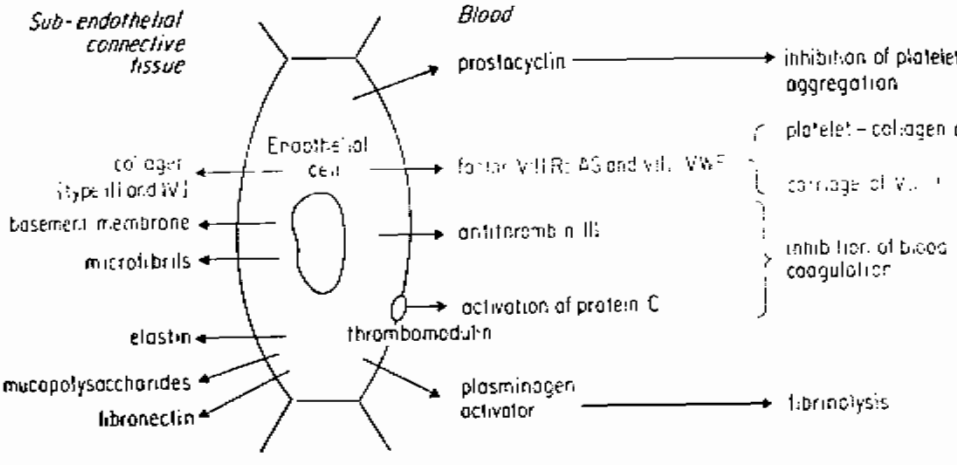
# Physiology Of Haemostasis

## PHYSIOLOGY OF HAEMOSTASIS

Haemostasis is divided into the following phases:

1. Vascular phase. 2. Platelet phase. 3. Plasma phase.

### Vascular Phase




The role of the endothelial cell in protecting the blood from coagulation and platelets from subendothelial aggregating substances. Quotted from A.V. Hoffbrand & J.E. Petit (eds). Essential Haematology, p.206, 1984.

Vessels with vascular coat contract following injury, thus assisting haemostatic plug formation by reducing blood flow. Vasoconstriction occurs, however, even in the microcirculation in vessels without smooth muscle cells (Hamberg et al., 1975) due to the release of vasoactive

substances from the platelets which are serotonin and thromboxane $A_2$.

The endothelial cells play an active role in haemostasis as they contract following injury or exposure to bradykinin, serotinin and histamine (Stemmmerman, 1974). It also synthesis and secretes at least three substances which are involved in the formation and localization of the haemostatic plug. These are von Willebrand factor, prostacyclin and plasminogen activator.

Von Willebrand factor (VII : vWF) is part of a molecular complex which also possesses factor VIII clotting activity (Bloom, 1977). It is involved in the adhesion of platelets to subendotheluim as it can bind to collagen and platelets contain a surface receptor for it. (Bolhuis et al., 1981).

Prostacyclin (PG $I_2$) is synthesized from arachidonic acid in the endothelial cells; it is a powerful inhibitor of platelet aggregation (Moncada et al., 1976) and prevents platelet deposition on normal vascular endotheluim. Plasminogen to plasmin which in turn lysis fibrin (Davidson, 1977).

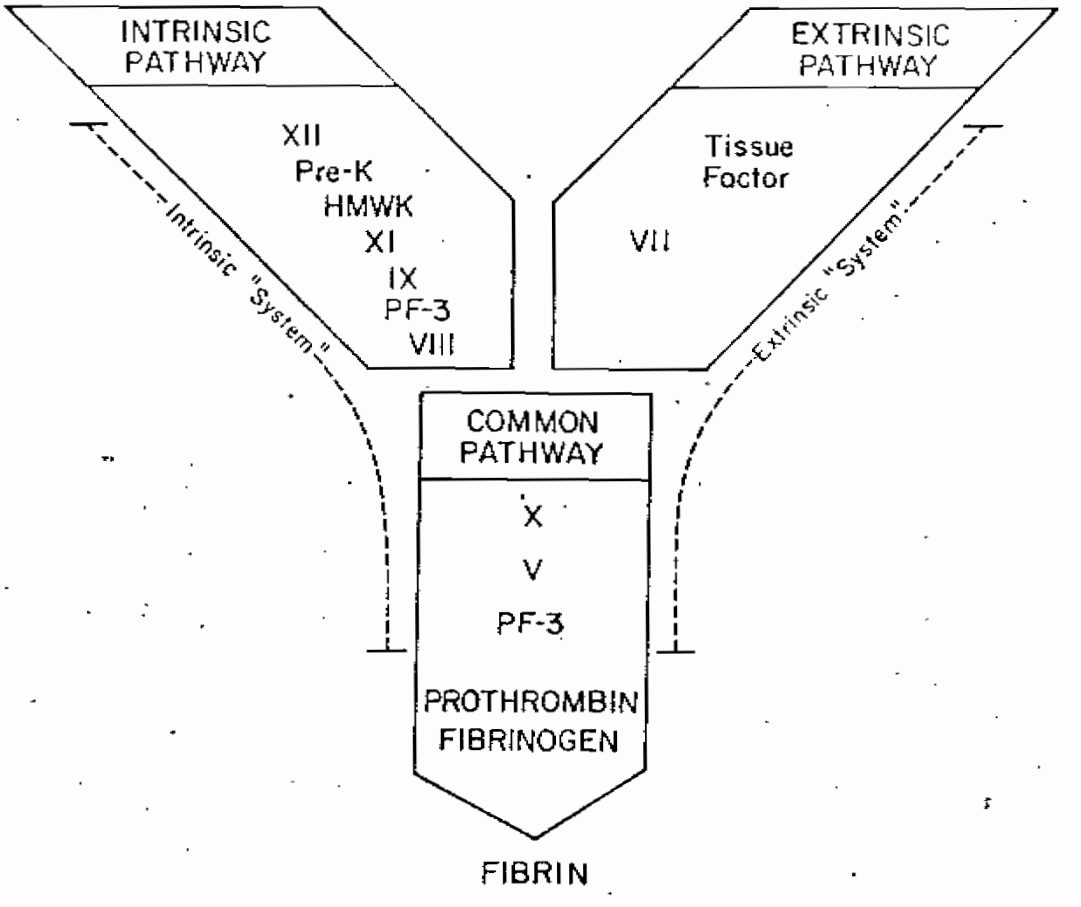
## Physiology of Blood Coagulation

### Plasma Phase

The cascade or waterfall hypothesis, views coagulation as an interlinked sequence of pro-enzyme to enzyme transformation. Coagulation factors, which normally exist in the plasma as inert precursors, are transformed into enzymes then convert the precursor next in line into its enzymatic form. Each coagulation factor thus acts first as a substrate and then as an enzyme (Wintrobe, 1982).

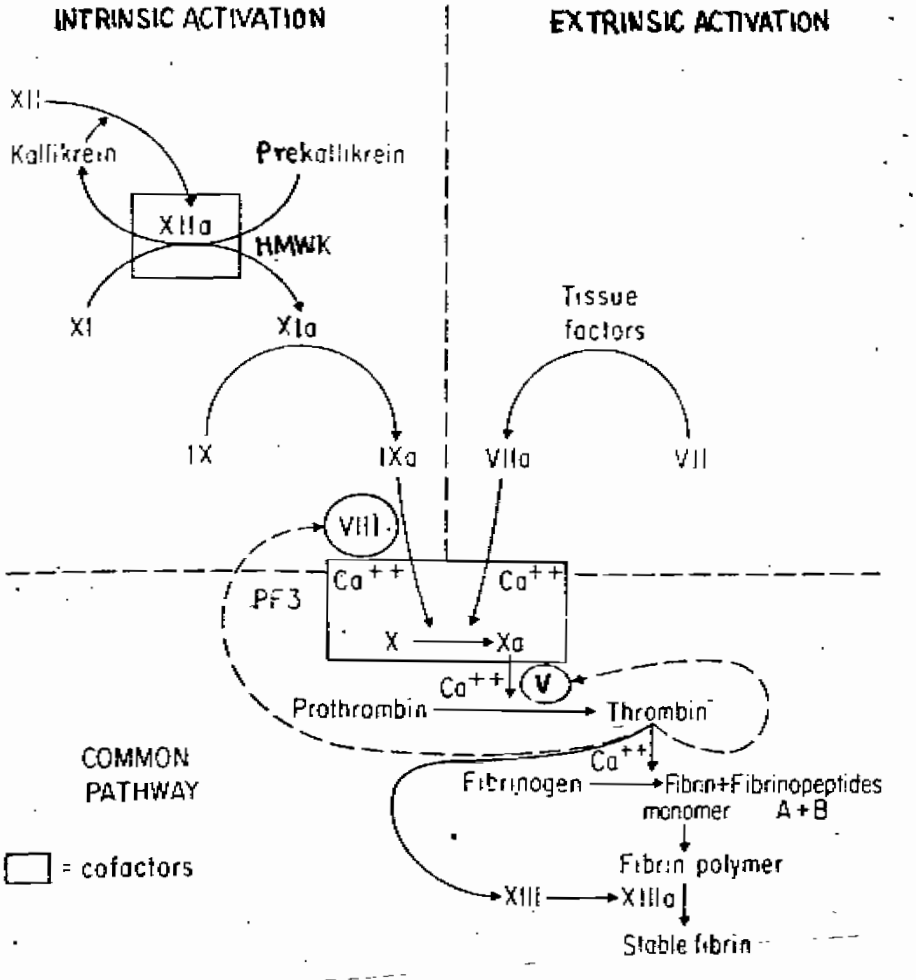
As seen in figures (p. 6 & 7) , there are two pathway for the initiation of coagulation under physiologic condition. These are termed the intrinsic and extrinsic system, and both converge on factor X , from which they share a common route to fibrin formation. Following tissue injury, the tissue activators produce small amounts of thrombin, which in addition in producing fibrin will greatly accelerate the intrinsic pathway by activation of factors VIII and V (Hoffbrand & Petit, 1984).

## PATHWAY OF COAGULATION




Pathways of coagulation. The terms intrinsic system and extrinsic system are widely used with reference to the reaction indicated by dashed lines. The following abbreviation are used: PF3, (platelet factor 3), Pre - K, (prekallikrein), HMWK, (high molecular weight kininogen). Quotted from Wintrobe Cl. Haematology, 1981.

## THE PATHWAYS OF BLOOD COAGULATION




Quotted from A.V. Hoffbrand & J.E. Petit (eds). Essential Haematology, p. 206,1984.