FACTORS AFFECTING THE PATENCY RATE OF MICROVASCULAR ANASTOMOSIS

Thesis

Submitted for partial fulfilment of the

Master degree

in general surgery

By

Ahmed Mohamed Salah El Badaway

M.B., B.ch.

Supervised by

Prof. Dr. Hassan Adel Badran

Professor of Plastic and Reconstructive Surgery Unit

Dr. Mostafa Mohamed Hemeda

Assistant Professor of Plastic and Reconstructive Surgery Unit.

Faculty of Medicine

Ain Shams University

ACKNOWLEDGEMENT

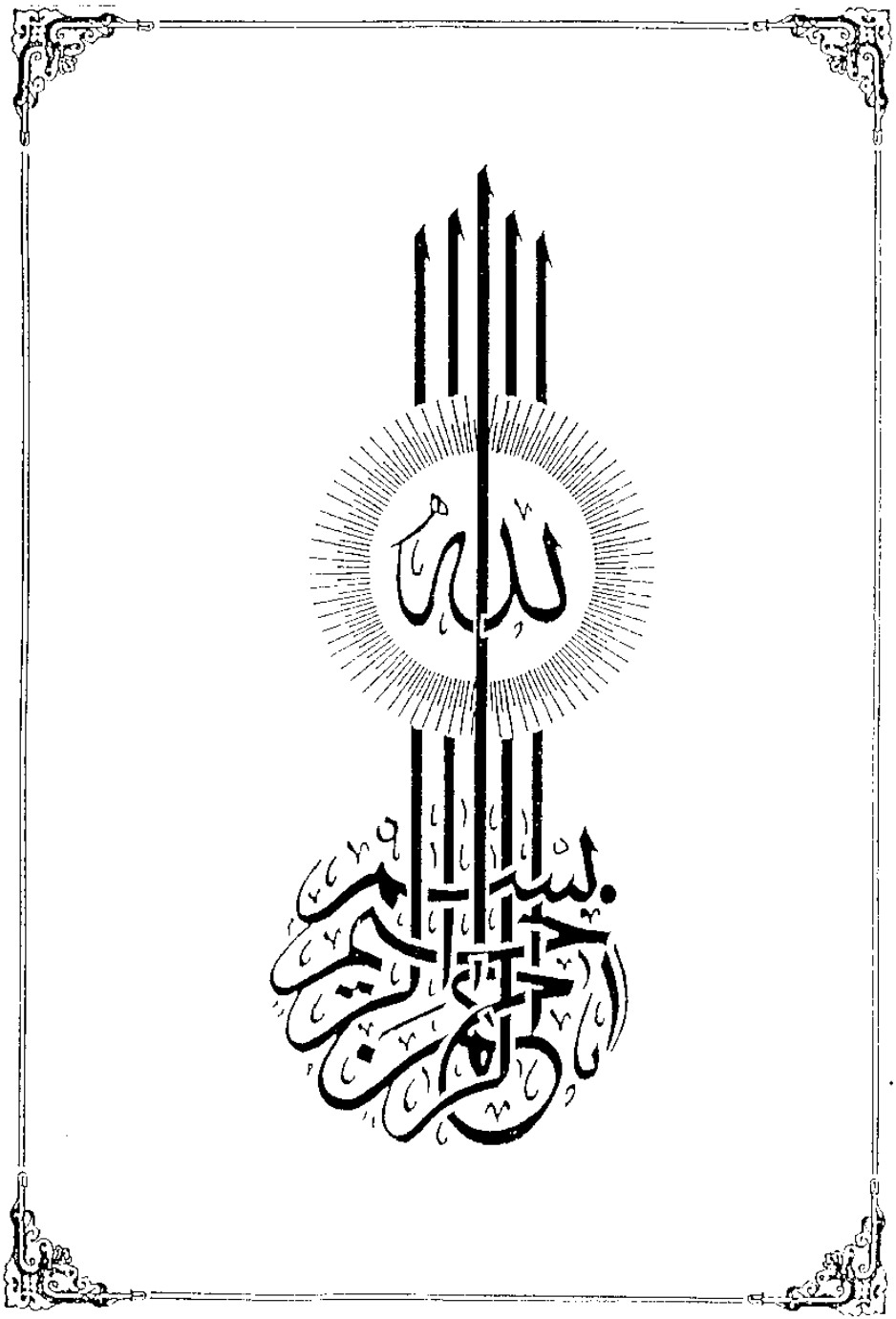
I would like to express my sincere gratitude and appreciation to **Prof. Dr. H.A. Badran** for his valuable help, effort and encouragement. His critical guidance and advice were invaluable.

I am faithfully grateful to **Dr. M.M. Hemeda** for his unique cooperation, suggestions, and encouragement throughout the work.

I wish also to express my deepest thanks to **Prof. Dr. M.M. Nafeh**, Professor and Head of our plastic and reconstructive surgery unit for his great encouragement and help.

I owe much to all the members of plastic and reconstructive surgery unit, Ain Shams University, especially to **Dr. M. Sherif, Dr. M. Khaled** and my colleague, **Dr. E. Eleish.**

A. El Badawy



CONTENTS

Introduction

Review of Literature

Physiology of hemostasis

Hemostasis is the spontaneous arrest of bleeding from damaged blood vessels. When a blood vessel is severed or ruptured, hemostasis occurs in three phases termed : vascular, platelet and coagulation.

(1) Vascular phase

Vascular spasm occurs immediately and lasts for 20 minutes to half an hour, during which the ensuing process of platelet plugging and blood coagulation can take place.

The degree of vascular spasm is proportionate to the type of trauma. This explains why sharply cut blood vessel usually bleeds much more than the vessel ruptured by crushing (Guyton, 1976).

(2) Platelet phase

Platelets are minute rounded or oval discs about 2 microns in diameter. They are fragments of megakaryocytes present in bone marrow. The normal concentration of platelets in the blood is between 200,000 and 400,000 per cubic millimeter.

Role of platelet in hemostasis :

1- Formation of platelet (hemostatic) plug which is important in hemostasis.

2- Plug any abnormally large gaps between endothelial cells, thus helping to maintain the normal vascular permeability (O'Brien, 1977 b).

3- Able to recognise any foreign material in the blood

stream and cover it with a layer of platelets to form an amorphous non-thrombogenic coating over the surface (Guyton, 1976).

The platelet phase has been previously described as being composed of adhesion, release reaction and aggregation.

* *Adhesion:*

Within seconds blood platelets come in contact with exposed collagen of the injured vessel by a process called platelet adhesion. Certain substances are present or are produced at sites of vascular damage, can produce platelet transformation. These substances are collagen, adenosine diphosphate (ADP), serotonin (5HT), adrenaline, and thrombin. If it comes into contact with one of these substances, a platelet instantaneously throws out many long, thin pseudopods (Acland, 1972 a).

The pseudopods have bulbous tips, which are sticky (Warren, 1971). In this altered state the platelets will stick, both to other sticky platelets, and to any site of damage where the smooth lining of the vessel is disturbed. This change in the platelet is reversible (Born, 1962). After a time the pseudopods will slowly withdraw and the platelet will slowly revert to its previous unsticky condition (T'Sao, 1970).

* *Release reaction:*

Adhesive platelets then discharge into the space around themselves, substances which have the property of making other platelets sticky (Day and Holmsen, 1971). These substance are ADP, 5HT and adrenaline. A platelet which has been provoked into producing a release reaction probably does not return to normal but undergoes irreversible changes. However, it should be noted that a

relatively strong stimulus is required to produce the release reaction (Born, 1962). A weak stimulus only makes the platelet stick, with no preceding release of its powerful chemical contents.

- ***Aggregation:***

Platelets then aggregate to form an enlarging platelet mass (Mustard and Feltham, 1970 a) and as the, lose their individual membranes, a viscus mass is formed (termed viscus metamorphosis). Thus a platelet plug is formed producing temporary hemostasis. If the rent in a vessel is small, the platelet plug by itself can stop blood loss completely, but if there is a large hole, a blood clot in addition to platelet plug is required to stop bleeding (Guyton 1976).

Control of platelet aggregation : There are two classes of prostaglandins which control platelet aggregation, Thromboxane-A2 and prostacyclin. Thromboxane A2 (TXA 2) is synthesized by the aggregated platelets and stimulates further aggregation. This is the most potent inducer of platelet release and aggregation. Prostacyclin A2 (PGI 2) is synthesized by the vessel wall and inhibits platelet aggregation (Kayser, 1983). Moncada and Vane (1978), believe that there is a balance between the activities of prostacyclin and thromboxane-A2. If intimal damage occurs, Prostacyclin generation is reduced in favour of an increase thromboxane-A2, and platelets then adhere to the defect. (Fig. 1) shows the detailed mechanisms of production of prostacyclin and thromboxane-A2.

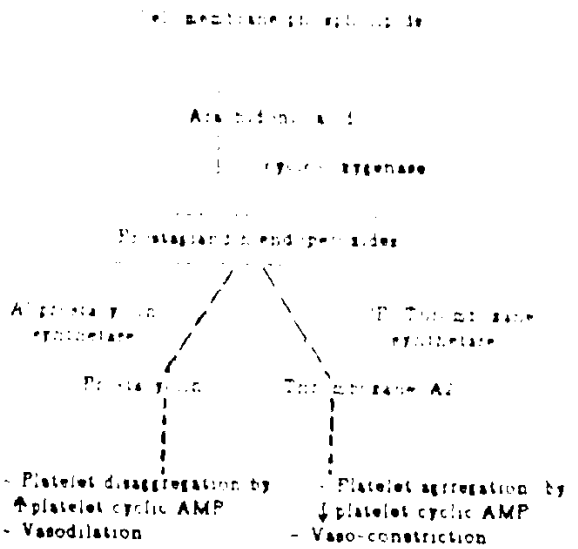


Fig 1 The mechanism of production of prostacyclin and Thromboxane-A2 [Emerson et al 1981]

A] The endothelial cells of blood vessels contain the enzyme prostacyclin synthetase Bunting and his colleagues [1976] believe that prostaglandin endoperoxides are brought to the vessel wall by blood platelets They are released, interact with the enzyme, and prostacyclin is generated

(7) Blood coagulation

[illegible] wall [illegible] completed within [illegible].

For achievement of a 'permanent' hemostasis, the [illegible] platelet plug must be reinforced by fibrin. This reinforcement is initiated by the local stimulation of coagulation process through an intrinsic or an extrinsic pathway, or both. This stimulus leads to a coagulation cascade, producing formation of fibrin, which provides the physical framework for all [illegible] clots. ([illegible], 1985).

* The physical events of this process are illustrated in Fig 2.
* The chemical events of this process will be discussed under the mechanism of blood coagulation.
* Fibrous organization of the blood clot

Once a blood clot is formed, an ingrowth of fibroblast along the scafolding of fibrin reparis the vacular rent permenantly (Gutyton, 1976).

Mechanism of blood coagulation :-

The mechanism was presented in 1964 by Mc Farlane. His hypothesis stated [illegible] of procoagulase to coagulase [illegible].

Coagulation factors, which normally exist in the plasma as inert precursor (Fig. 1), are transformed into enzymes when activated. These 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. Several revisions of the coagulation " cascade " have been made because of new informations. Despite continuing disagreement concerning details of individual steps, the essential core of the cascade hypothesis remains widely accepted.

Blood coagulation is initiated by two fundamentally different mechanisms termed, the intrinsic and extrinsic, that "converge" by activating a third common pathway leading to fibrin formation which converts the loose temporary plug into a definitive clot (O'Reilly, 1985).

(A) The intrinsic mechanism

It is initiated by trauma to the blood itself in the form of exposure of blood to the collagen fibres underlying the endothelium of the blood vessel. This results in activation of factor XII and release of platelet phospholipids. The former starts the intrinsic pathway while the latter plays a role in subsequent clotting reactions. (Guyton, 1976).

Thus factor XII undergoes contact activation and becomes bound to surfaces. This surface - bound fator XII

undergoes proteolytic activation by kallikrein (Ka) in the presence of high molecular-weight kininogen (HMW.K). Activated factor (XIIa) constitutes an arm of a feed back loop and activates more Ka from prekallikrein (pre-K or Fletcher factor), in the presence of HMW.K. (Colman, 1975; Webster, 1979). Factor XIIa in the presence of HMW-K also activates factor XI. Factor XIa in the presence of Ca^{++} proteolytically activates factor IX to IXa. Factor VIII, factor IXa Ca^{++} and phospholipid micelles (PL) from blood platelets, form a lipoprotein complex with factor X and activate it.

(B) The extrinsic mechanism

It is initiated by trauma to the tissues outside blood vessels which results in liberation of tissue thromboplastin (factor III), which activates blood coagulation at the level of factor X.

Factor XIIa, Xa and Ka liberated from the intrinsic system activates factor VII to VIIa. Factor VIIa., Ca^{++}, tissue thromboplastim (III), and factor X form a lipoprotein complex that results in activation of factor X.

(C) The common pathway of coagulation

Factor V, factor Xa, Ca^{++} and PL also form a lipoprotein complex with factor II (prothrombin) and activate it to IIa (thrombin).

In seconds, thrombin splits two small pairs of peptides off the large fibrinogen (I) molecule, followed by rapid non covalent aggregation of soluble fibrin monomers (I). Factor XIII, activated by thrombin to XIIIa, crosslinks adjacent fibrin monomers (I) covalently to form the insoluble fibrin clot (I").

The previous mechanism is the most recent hypothesis of blood coagulation and is illustrated in fig 4. (Ratnoff, 1981; Zwaal and Hemker, 1982). From the previous mechanism, it is noted that the extrinsic mechanism is explosive in nature (activated within seconds) because the early time consuming reactions are by-passed. Its speed of occurance is limited only by the amount of tisue factor released from the traumatized tissues. So with sever tissue trauma clotting can occur in as little as 15 seconds.

On the other hand, the intrinsic pathways is much slower to proceed (requires 1-7 minutes). However, both pathways must be intact for adequate hemostasis (O'Reilly, 1985).

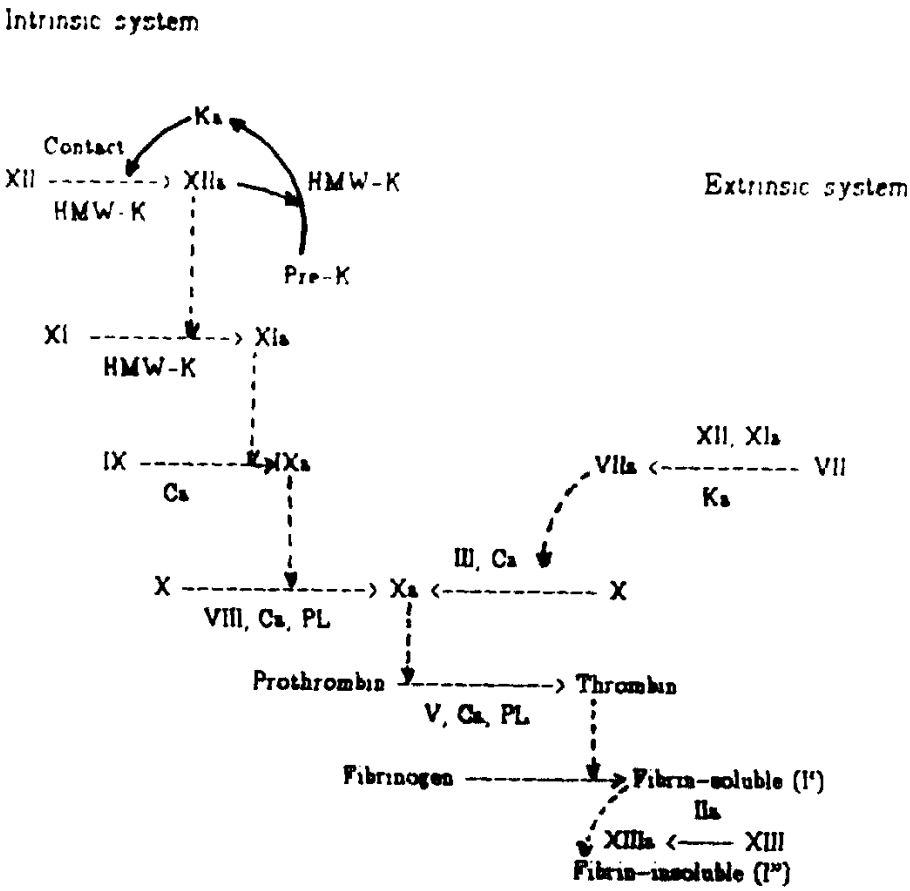


Fig 4 Chemical events of blood coagulation (O'Reilly, 1985)