PLATELET FUNCTION DURING AND AFTER NORMAL CHILD BIRTH

THESIS

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BY

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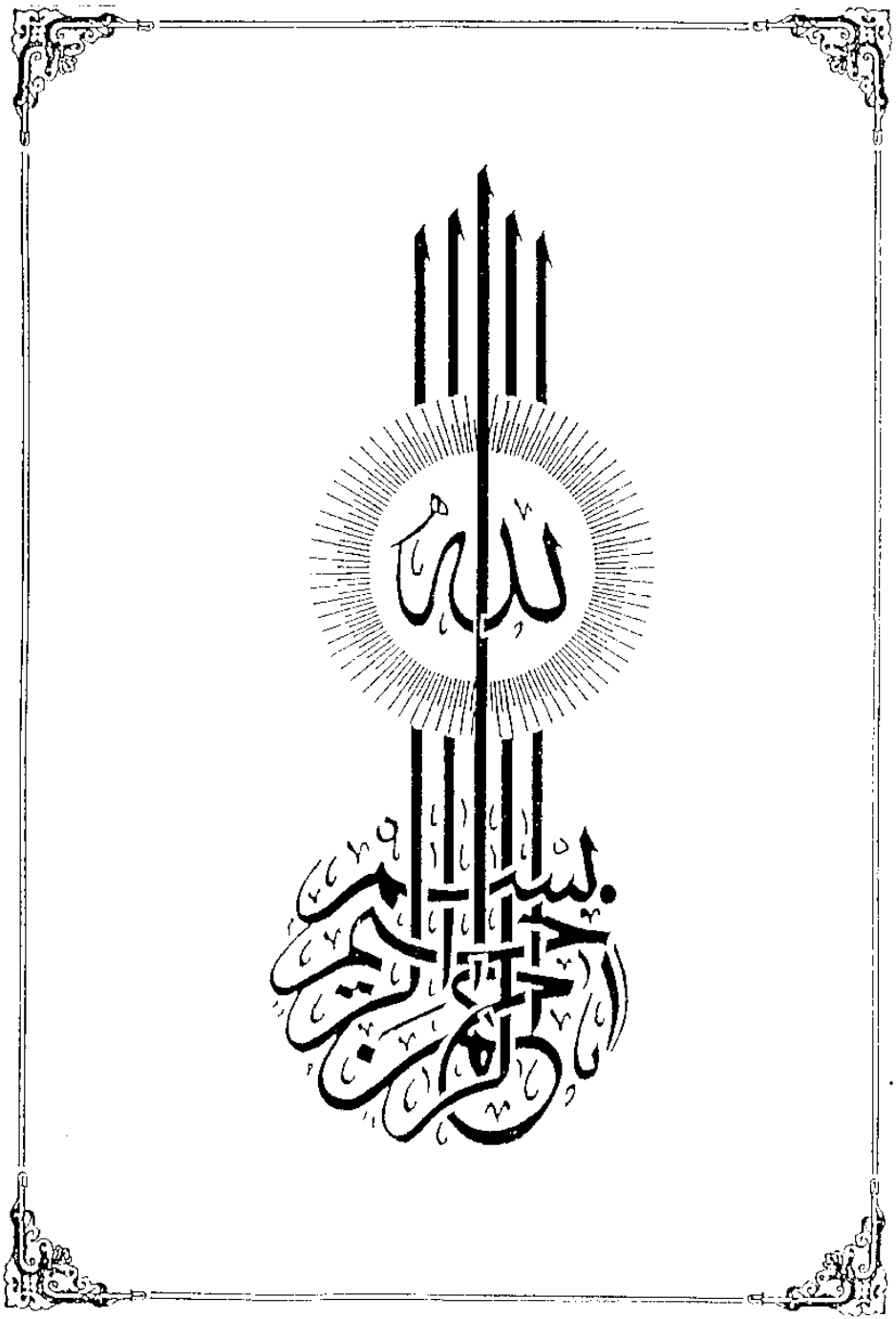

LIST OF ABBREVIATIONS

A	= Angle of aggregation.
ADP	= Adenosine Diphosphate.
AT	= Aggregation time.
CT	= Clotting time.
D	= Duration of aggregation.
EDTA	= Ethylene Diamine Tetre Acetic Acid.
HR	= Hour.
Max.Agg.	= Maximum Aggregation.
Min.	= Minute.
OD	= Optical Density.
PA	= Platelet Aggregation.
%Disagg.	= Pereent Disaggregation.
PF_3	= Platelet Factor 3.
PRP	= Platelet Rich Plasma.
PRT	= Plasma Recalcification Time.
SD	= Standard Deviation.
SEC	= Second.

NOMENCLATURE OF BLOOD CLOTTING FACTORS

Factor I = Fibrinogen.

" II = Prothrombin.

" III = Tissue Thromboplastin.

" IV = Calcium.

" V = Labile Factor, Proaccelerin.

" VII = Stable Factor, Proconverrin.

" VIII = Antihaemophilic globulin.

" IX = Plasma thromboplastin component (PTC) or christmas factor.

" X = Stuart - Prower Factor.

" XI = Plasma thromboplastin antecedent (PTA).

" XII = Hageman Factor.

" XIII = Fibrin stabilising Factor.

I N D E X

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Arrest of bleeding after delivery is a vital physiological process of extreme importance. This was considered for a long time as a myometrial function . A study of the coagulation and fibrino-lytic systems during normal parturition , showed a striking activation of the coagulation mechanism during and after placental separation.

This enhanced capacity towards maximum coagulation prepares the body to meet the local challenge in the uterus. The role of platelets in this challenge was not fully studied before. The aim of this work is to study the platelet functions during and after normal child-birth , and to correlate the findings with the amount of blood loss during this period.

THE HEMOSTATIC MECHANISMS

Hemostasis is the mechanism by which animals with a vascular system are protected from death by bleeding after an injury.

Physiological hemostasis depends on the following sequence of processes:

i. The Vascular Mechanism:

In the capillaries and the smallest venules, hemostasis is accomplished by direct adhesions of endothelial surfaces (Chen and Tsai, 1948). When a larger blood vessel is injured any smooth muscule in the wall contracts. This is achieved by sympathetic vaso-constrictor fibres supplying the smooth muscles in the vessel wall (Cruz et al, 1963). Contraction of the vessel is reinforced by platelet aggregates and by the release, from the platelets, of the powerful vasoconstrictor serotonin (Zucker and Rapaport, 1954).

ii . Role of Platelets:

The platelets adhere to the injured vascular wall particularly to collagen fibers (Hathaway,1971), with which they interact, in the presence of divalent cations (Sneddon, 1973), to release some of its constituents. Of

the released constituents, the most important are ADP (Ireland, 1967), PF 3 (Speat and Cintron, 1965), and serotonin (Hensen et al, 1973). ADP induces platelet aggregation (Speat and Zucker, 1964), which is still permeable to the blood stream and is reversible (Born, 1962), This permeable hemostatic plug is transformed to an impermeable one by thrombin (Hovig,1962).

In the case of large vessels, although the vascular and platelet elements are important in limiting the initial loss of blood, the formation of a fibrin clot plays the major role in hemostasis.

iii. Blood Coagulation Mechanism:

The classic theory of blood coagulation as described by Morawitz, (1905), can be summarized by:

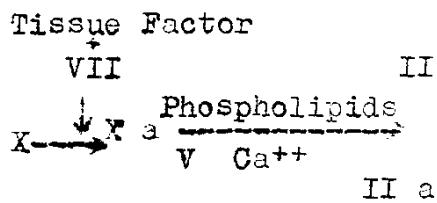
(1) Prothrombin $\xrightarrow[\text{ionic calcium}]{\text{thromboplastin}}$ thrombin.

(2) Fibrinogen $\xrightarrow{\text{thrombin}}$ fibrin.

Since the time of Morawitz, many other factors had been discovered for which the Roman numerical system of nomenclature had been applied.

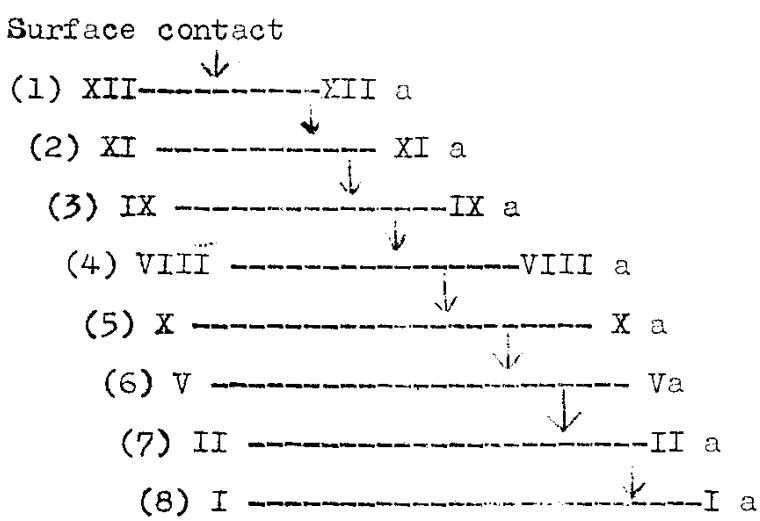
It is now generally accepted that there is an extrinsic (tissue-activated) system and an intrinisic (contact-activated system) in the coagulation mechanism. Subendothelial connective tissue; exposed in injured blood vessels, activates the intrinsic pathway, whereas tissue factor, made available in injured tissue, activates the extrinsic clotting pathway. Both coagulation pathways, once activated, facilitate the conversion of prothrombin to thrombin with the result formation of fibrin clot.

The extrinsic system was studied by Biggs et al, (1953), Nemerson and spaet, (1964), Williams, (1966), Nemerson (1966 & 1969), and Leveson and Esnouf, (1969). The tissue extract was found to contain a protein and a lipid component. The protein component has a peptidase activity (enzymic activity). Tissue extracts from which the phospholipid had been removed, activates factor X in the presence of factor VII. Phospholipid was then required for the interaction of X a, factor V and calcium to form a complex which converted prothrombin to thrombin.



Many theories had been put forward to explain the way in which the factors might interact in the intrinsic system. Of the various theories, the sequential theory was a useful one because it was made up of clearly stated hypothesis which could be tested by experiments, thus it was useful for the diagnosis and successful treatment of hemorrhagic states.

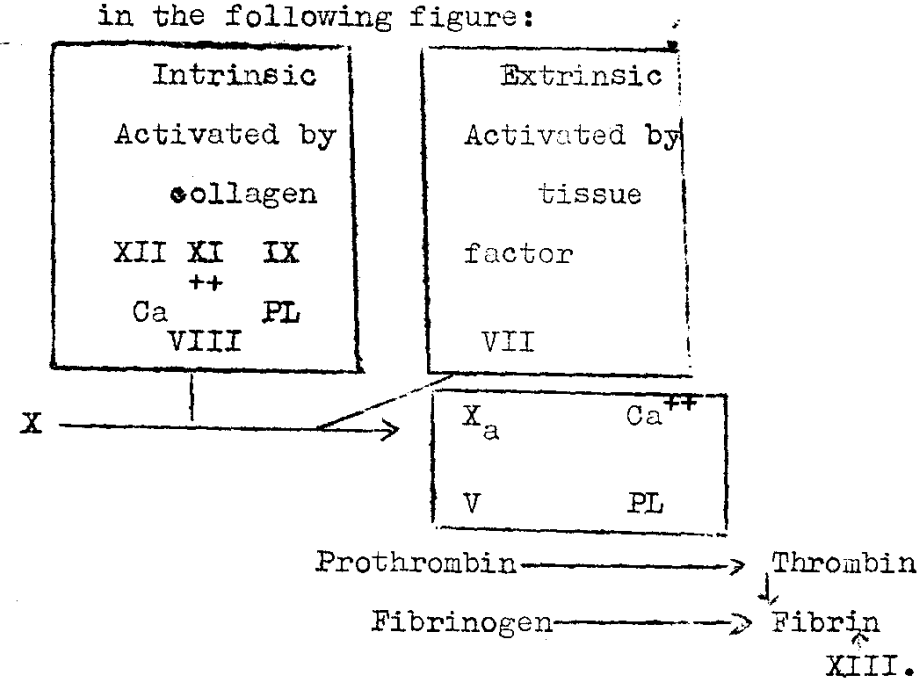
It had been suggested in Macfarlane's cascade theory, (1964), and Davie and Ratnoff's waterfall theory (1964), that each step involved two factors, an enzyme acting on an inactive form of clotting factor, a proenzyme. The enzyme converted the proenzyme into its enzymic form. This second enzyme then activated the next proenzyme and so on. The cascade is represented as follows:



Calcium is needed for all steps except step (I) and step (8). A phospholipid usually derived from platelets, was essential at step (6) or possibly (7), and another was required at step (4), (Macfarlane et al 1964).

From the work of Macfarlane and Ash, (1964), it was supposed that factor X was activated in a similar manner both by the intrinsic plasma system and tissue thromboplastin and a common product was the enzyme X a.

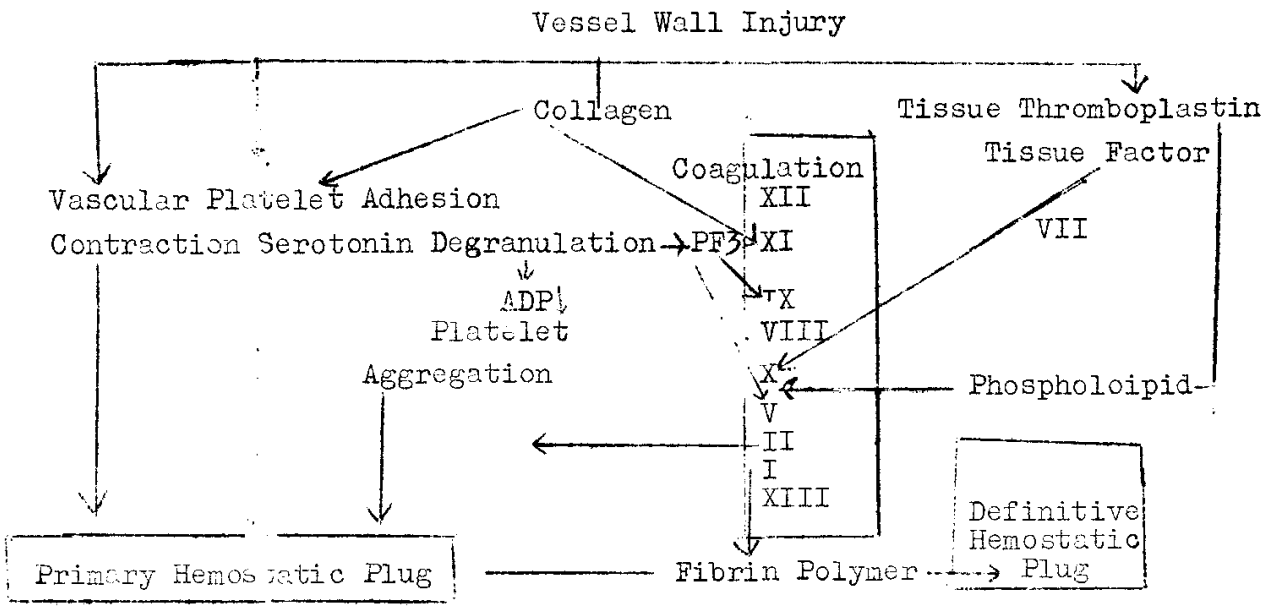
A blood coagulation scheme, linking both the extrinsic and intrinsic mechanisms together is represented in in the following figure:



" From the Medical Clinics of North America. P.1097, July 1973 " (pL = Phospholipids).

Koniski and Lorand, (1966), showed that factor XIII was found normally in the plasma and platelets as a proenzyme which in the presence of thrombin and calcium ions was converted to an enzyme, active transmidase. Pisano et al, (1968), found that this enzyme, by a trans-amidation reaction, was capable of cross-linking fibrin monomers to convert soluble fibrin clot to and insoluble fibrin clot.

The components of the hemostatic mechanism are illustrated in the following figure:



Components Of The Hemostatic Mechanism Modified After Deykin , (1967), And Davie And Associates, (1969). By Bleyer, M.A. , Hakemi, N., Shepard , R.H. : J. Pediat., 79:839 , 1971.