POST OPERATIVE CHANGES OF PLATELETS

An Essay

Submitted For Partial Fulfilment of

M. Sc. Degree In Clinical Pathology

BY

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1987

ACKNOWLEDGMENTS

This essay was prepared in the Clinical Pathology department Faculty of Medicine, Ain Shams University under the supervision of Prof. Dr. TARIF HAMZA SALAM to him I wish to express may deepest feelings and sincere gratitude for his generous help, advice, continous guidance and encouragement .

It does not set out to be a comprehensive text book, but it should be regarded as a review of literatures and complementary to such text books rather than as a substitute for them .

I am grateful to Prof. Dr. NEHAYET MAHMOUD AZMY for the invaluable time devoted and sternuous efforts exerted to teach me along these years.

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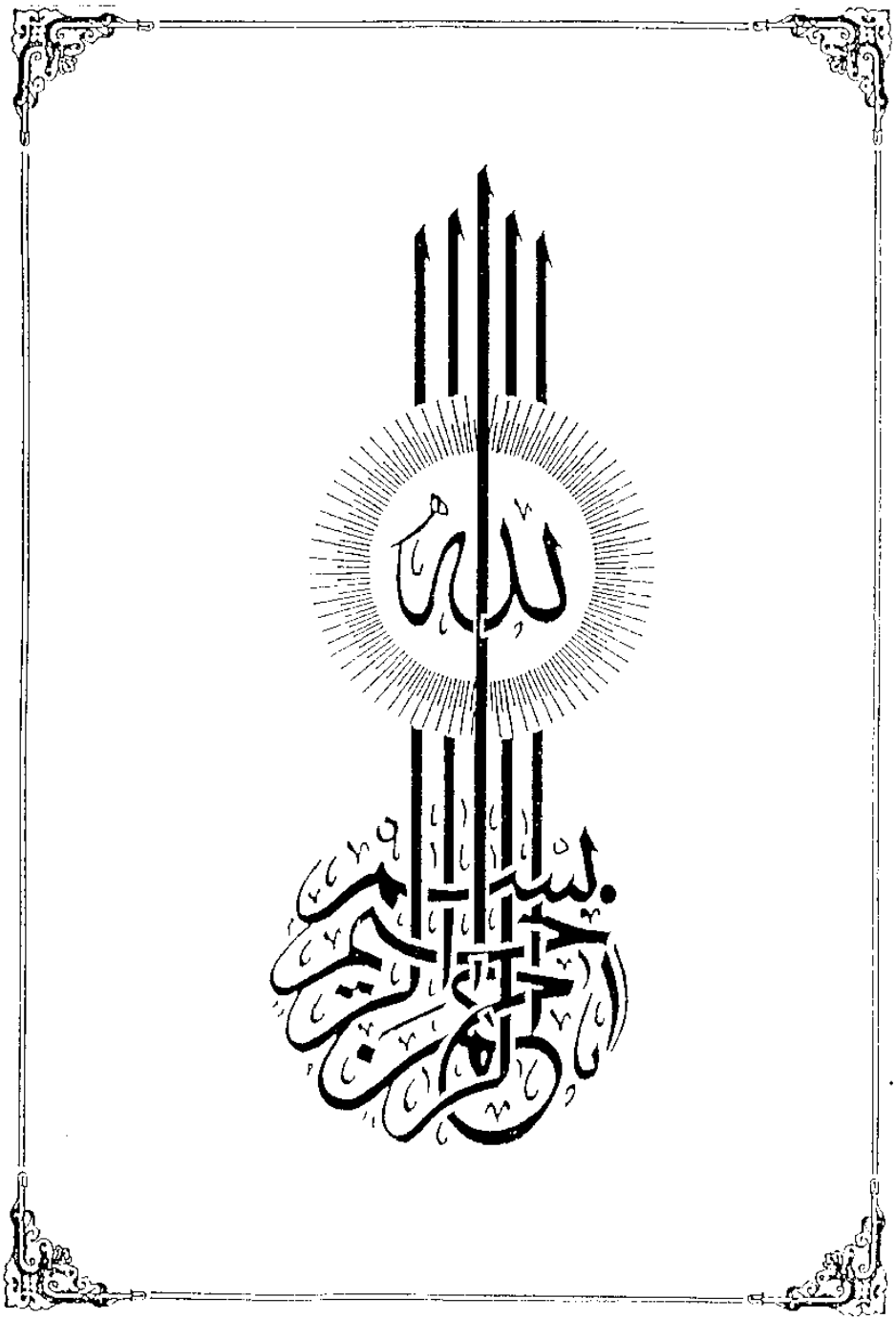
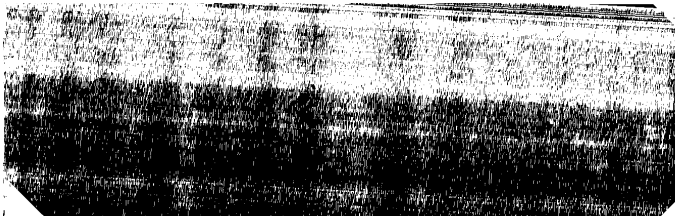
1987





PLATELET MORPHOLOGY AND STRUCTURE

The blood platelets in man circulate as flattened discs at a concentration of $250 \times 10^{9}/L$ (range 150,000 - 400,000 platelets/ Cmm). The morphology varies greatly depending on the methods by which they are examined, the anticogulant employed and the temperature (Maupin, 1969).

Platelets are the smallest of the formed elements of human blood . In quiescent stage, they circulate as small, enucleate, biconvex, discoid cells having a mean diameter of 2 - 4 microns (Cerash et al., 1977 and Paulus et al., 1982). By rheo-optical methods, while platelets rotating in suspension, the average dimentions are 3.6 ± 0.7 um in diameter and 0.9 ± 0.2 um in thickness (Frojmovic and Panjwani, 1976).

In wet preparation, platelets are colourless moderately refractile bodies with few central granules (Frojmovic, 1978).

Under dark illumination they are translucent and reveal a sharp contour . A few immobile granules

are present in the center of the cell. In polychrome stained blood smears, platelets appear round, oval, or rod shaped . Azurophilic granules are seen in a hyaline light-blue cytoplasm. These granules may be so tightly packed in the central portion giving the appearance of a nucleus (Projnovic and Panjwani,1976).

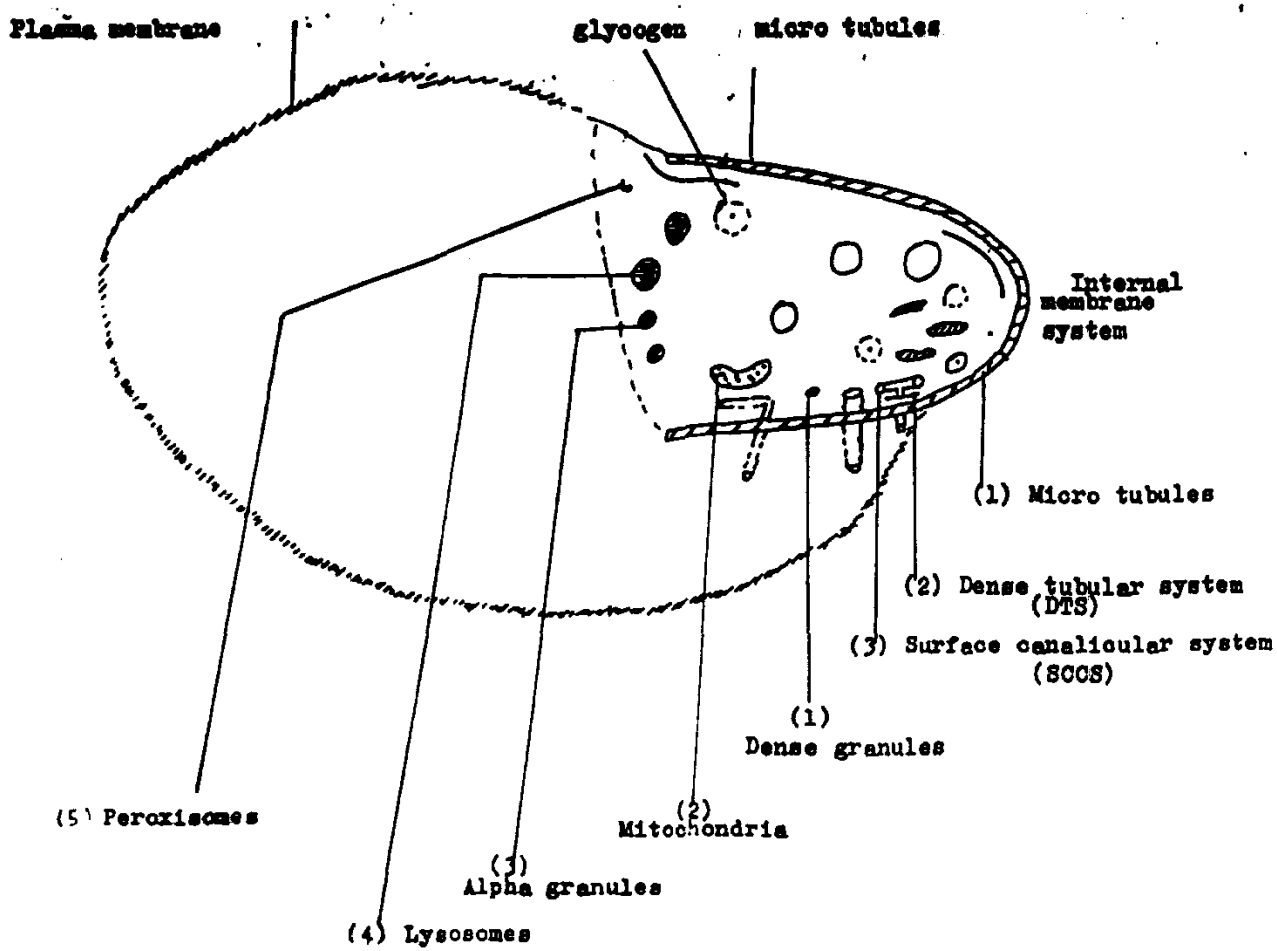
Ultra structure of platelets :

By electron microscopy there are 3 major structural zones within the platelet .

- A peripheral zone, which is the site of adhesion and aggregation reactions .
- A sol-gel zone or matrix, containing an irregular network of microfilaments and microtubules that support the platelet discoid shape and contractile mechanism .
- An organelle zone embeded in the matrix which contains all structures related to the metabolic processes, storage and release of products .

An additional feature of platelet morphology is the membrane system which constitutes a fourth functional zone in blood platelets (White et al., 1981).

The main features of platelet ultrastructure as revealed by electrone microscopy are depicted diagrmatically in Figure 1.



1-5 Organells

Fig.(1) Diagramatic representation of a resting human platelets (NICHOLS et al., 1981).

At least five major glycoproteins (GPI to GPV) have been well characterised (Anonymous, 1981). GPI is necessary for normal adhesion, GPII, III for normal aggregation.

The surface glycoproteins contain terminal sialic acid molecules contributing to a large negative surface charge which could aid by electrostatic repulsion in preventing platelets from sticking to each other or to normal intact endothelium. Loss of surface sialic acid or glycoproteins appears to be the principle mechanism of platelets senescence in vivo (Greenberg et al., 1979).

The glycocalyx is also rich in carbohydrates which are provided by glycoproteins glycolipids and glycosaminoglycans or mucopolysaccharides (Nichols et al., 1981).

More over, protein antigens are localised in the exterior coat. This coat is the site of adhesion and aggregation as well as non specific adsorption of plasma constituents such as fibrinogen and factor VIII (Crawford and Taylor, 1977).

B) The unit membrane, a typical trilaminar membrane, consists mainly of a phospholipids bilayer with transmembrane protein components randomly dispersed. It protects the intergrity of the platelet internal milieu and is intimately involved in the control or generation of the many specialised functional properties such as hemostasis (Schick, 1979), and acceleration of blood coagulation (Zwaal, 1978), and release of platelets factor-3 .

Other important components of the platelet unit membrane include the membrane endoenzymes, the enzymes involved in membrane transport and cyclic AMP metabolism (Crawford and Taylor, 1977). Unique morphologic features of the platelet plasma membrane include numerous intracellular invaginations to form the surface connected canalicular system .

C) The submembrane area, immediatly under the unit membrane , represents a transition between the peripheral zone and the sol-gel matrix of the hyaloplasm, because its structural elements appears closely associated with changes in the cell surface, the submembrane area is considered part of the peripheral zone (Steer and Wood, 1979).

It consists of fine filaments peripheral to the circumferential bundle of microtubules which help to support the platelet discoid shape in the quiescent stage participate in formation and stabilisation of pseudopodia and aid in retraction of surface projections during viscous metamorphosis (Zucker and Franklin, 1969).

Sol-gel zone :

The sol-gel zone or hyaloplasm comprises the viscous matrix inside the platelets .

It is a circumferential band of microtubules just inside the external membrane, it seems to serve as a skeletal frame to hold the discoid shape. Platelets contain large amounts of actin and myosin which forms a contractile elements called microfilaments are, in case of platelets, thrombosthenin(Gerrard and White, 1980).

Organell zone :

The matrix of the platelet contains many particles and granules, these include :

I. Dense granules : Human platelet dense granules contain calcium, ADP, ATP, pyrophosphate, serotonin , and possibly antiplasmin (Joist et al., 1976). About 65% of human platelet ADP and ATP are stored in the dense granules (storage pool) and are released on stimulation but are not readily exchanged with those of 35% of the cytoplasm which represent the metabolic pool (Holmsen and Weiss, 1979).

II. Alpha granules : These contain proteins that are also found in plasma, including fibrinogen, von willebrand factor ; fibronectin and coagulation factor V, and proteins that are specific for granules, including platelet factor 4 and B-thromboglobulin (Kaplan, 1981).

III. Lysosomes (White, 1971).

IV. Glycogen granules : Glycogen is a major component of platelets, providing a stored energy source (Akkerman, 1978).

V. Mitochondria (Hovig, 1968).

VI. Golgi apparatus .

PLATELET ACTIVATION

Platelet stimulation or platelet activation is a loosely defined term implying significant functional, biochemical and or structural alternation of platelets, not found in the unstimuluted and unexcited state. Such activation ordinarily requires metabolically intact platelets and is usually defined operationally by one or more of the following terms (Nichols et al., 1981).

Adhesion refers to platelet attachement or cementing to the wall of a blood vessel or to foreign surface . Shape change or viscous metamorphosis represents a rapid transformation of the smooth, discoid appearance of the resting platelets into a spherical form with pseudopodial extensions . Aggregation indicates non-immunologic cohesion of activated sticky platelets to one another, while agglutination is a term reserved for immunologic clumping .

Holmsen(1970) stated that release reaction refers to the secretion by platelets of certain substances stored in the intracellular organelles, this

reaction usually follows one or more of the activation processes noted above, and has been classified by Kaplan et al., 1979 , into sequential stages: Release I and Release II. Exocytosis of the dense bodies and alpha granules occur simultaneously and with similar dose response relationships whereas exocytosis of acid hydrolases from lysosomes is a considerably slower process and requires a higher degree of stimulation or excitation. Platelet procoagulant activities are mostly latent in resting platelets, but become manifest with platelet activation processes, serving ultimately to accelerate the generation of thrombin and the conversion of fibrinogen into fibrin. Primary hemostasis encompasses the interaction of the platelets with blood vessels and certain coagulation factors to form a hemostatic plug, it is to be distinguished from secondary hemostasis which mainly involves plasma coagulation factors and fibrin clot formation (Hoffbrand and Pettit, 1982).

Platelet retention reflects the progressive numerical diminution of the platelet content of whole blood exuding from a small wound or passing across a foreign surface . This phenomenon is thought to result

from several platelet activation processes including adhesion, shape change , aggregation and release reactions (Nichols et al.,1981).

When blood is exposed to injured tissue or a foreign surface, a striking transformation of platelets takes place . (Fig. 2) . The shape changes from discoid to spherical. Sequestrated Ca^{++} is released . Receptors for factor V and fibrinogen/fibrin appear on the surface . The contents of dense and a granules are secreted. Arachidonic acid, fatty acid that is present in platelet membrane is liberated and converted by cyclooxygenase into endoperoxides . The endoperoxides, in turn are converted to thromboxane A_2, a potent aggregating agent (Holmsen and Day, 1975). Platelets aggregate and fuse to form amorphous mass. They are enmeshed along with red cells, in a network of fibrin. The contractile elements of the platelets pull together the fibrin strands to which the platelets have adhered trapping the red cells and forcing serum, this phenomena is called "clot retraction" . Thus , retraction of a clot formed from shed blood in vitro is a simple measure of platelet function (Gerrard et al., 1980).