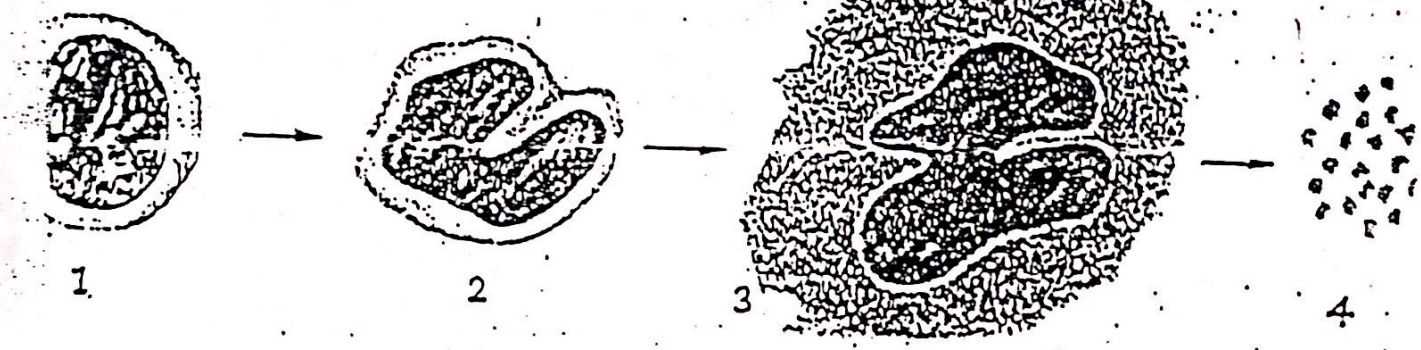


Fig. 2.5.3. Development of platelets — 1, promegakaryoblast 2, megakaryoblast 3, megakaryocyte 4, platelets

Platelets are developed from the giant cells called *'megakaryocytes' in the bone marrow*, whose diameter is usually around 100 μm. A single megakaryocyte can give rise to about 4000 platelets.

Normally, the bone marrow contains only about one day's reserve of platelets. Therefore, human beings are susceptible to develop thrombocytopenia more quickly than granulocytopenia or erythrocytopenia.

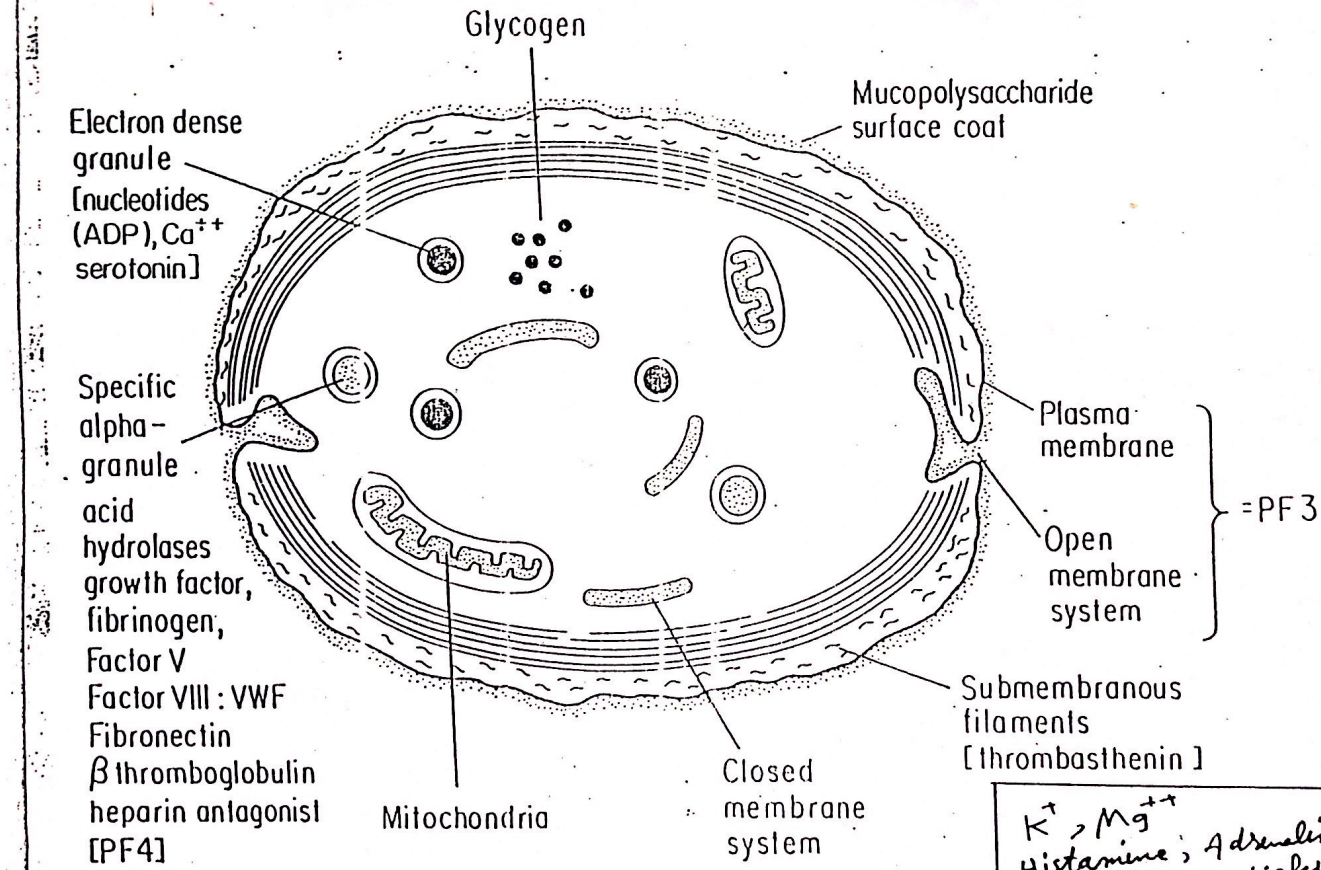


Fig. 11.2 Diagrammatic representation of the ultrastructure of platelets.

K^+, Mg^{++}
Histamine, Adrenalin
Albumin, Antiplasmin
Lipoproteins, Prostaglandins
Thromboxanes.

HEMOSTASIS

* Physiological hemostatic mechanisms are most effective in dealing with injuries in small vessels (arterioles, capillaries, venules).

* The bleeding from a medium or a large artery is not usually controllable by the body.

* Venous bleeding is less dangerous because veins have low blood pressure.

* If the venous bleeding is into the tissues, the accumulation of blood may increase interstitial pressure enough to eliminate the pressure gradient for continued blood loss.

* Accumulation of blood in the tissues can occur as a result of bleeding from any vessel type and is termed ***hematoma***.

NORMAL HAEMOSTASIS

The cessation of bleeding following trauma to blood vessels results from three processes: (a) the contraction of vessel walls; (b) the formation of a platelet plug at the site of the break in the vessel wall; and (c) the formation of a fibrin clot. The clot forms within and around the platelet aggregates to form a firm haemostatic plug. The relative importance of these three processes probably varies according to the size of the vessels involved. Thus, in bleeding from a minor wound, the formation of a haemostatic plug is probably sufficient in itself, whereas, in larger vessels. contraction of the vessel walls also plays a part in haemostasis. The initial plug is formed almost entirely of platelets but this is too friable on its own and must be stabilized by fibrin formation.

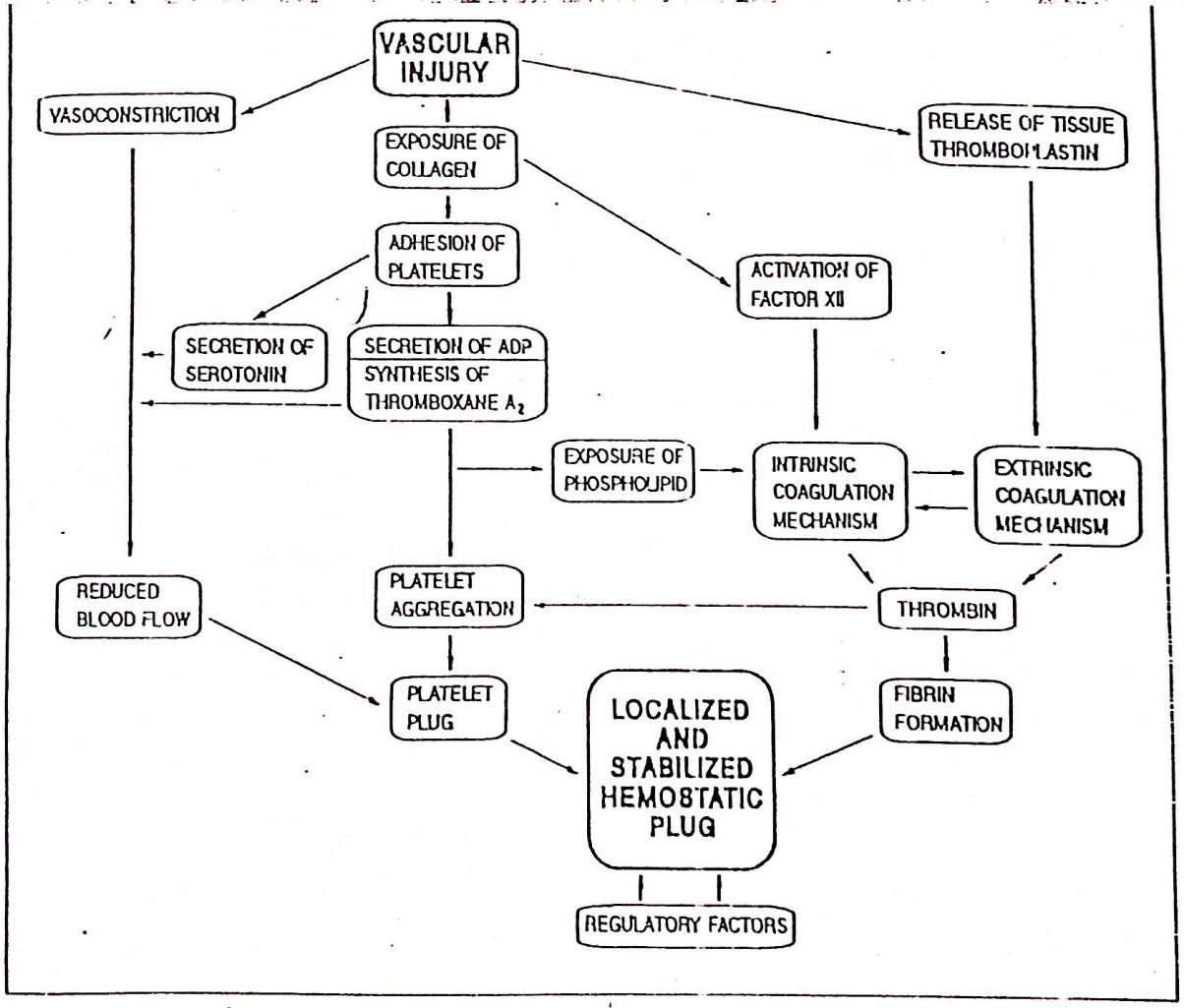
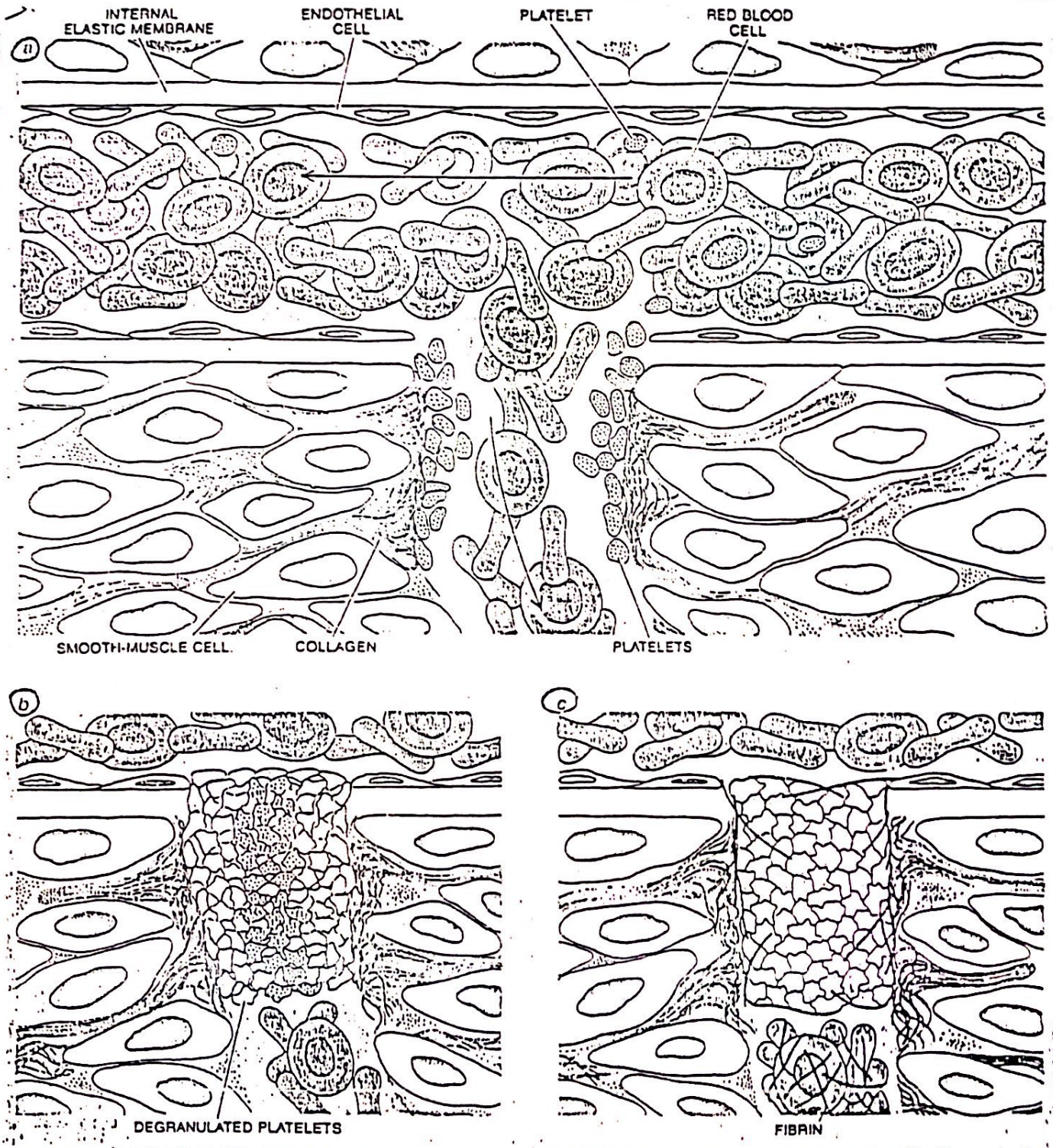


Fig. 25-4. Summary of the integrated hemostatic response to vessel injury. (See text description.)



ROLE OF PLATELETS IN HEMOSTASIS, or the stoppage of bleeding, is diagrammed. As blood begins to flow out through a cut in the vessel wall, platelets adhere to collagen in the wall (*a*). The platelets are thereby stimulated to secrete the contents of their granules, including ADP, and other passing platelets adhere to the first layer, building up a loose plug in the wound channel (*b*). Changes in the platelets and contact of blood with damaged cells convert the plasma protein prothrombin into the enzyme thrombin. The thrombin in turn converts fibrinogen into fibrin strands, which reinforce the platelet plug, and it also causes platelets to pack together more closely (*c*).

Platelet Function

The main function of platelets is the formation of mechanical plugs during the normal haemostatic response to vascular injury.

Central to this function are the platelet reactions of adhesion, release, aggregation & fusion as well as their procoagulant activity.

Platelet Adhesion:

This vital function is dependent upon a part of the factor VIII protein in plasma known as the von Willebrand factor which is part of the main fraction of the factor VIII molecule, factor. VIIIR:AG (factor VIII – related antigen).

Adhesion is also dependent on a platelet surface membrene glycoprotein.

F. VIII: Is a protein produced by endothelial cell & platelet.

F. VIII. Molecule is made up of several functional parts.

1. F. VIII:C refers to the coagulant portion of the molecule & represents the ability of the molecule to correct coagulation

2. F. VIIIR:AG makes possible platelet aggregation.

3. F. VIII:VWF that is required for normal platelet adhesion in hemostasis.

The Release Reaction.

Collagen exposure or thrombin action results in the release of ADP, serotonin, fibrinogen, lysosomal enzymes & heparin neutralising factor (platelet factor 4).

Collagen & thrombin activate platelet prostaglandin synthesis leading to the formation of a labile substance, thromboxane A_2.

This substance not only potentiates platelet aggregation but also has powerful vasoconstrictive activity.

The release reaction is inhibited by substances which increase the level of platelet cyclic AMP.

One such substance is the prostaglandin prostacyclin (PGI_2) which is synthesised by vascular endothelial cells.

It is a potent inhibitor of platelet aggregation & probably prevents their deposition on normal vascular endothelium.

Platelet Aggregation

Released ADP & thromboxane A_2, cause additional platelets to aggregate at the site of vascular injury.

ADP causes platelets to swell & encourages the platelet membranes of adjacent platelets to adhere to each other.

Platelet Procoagulant Activity

After platelet aggregation & release the exposed membrane phospholipid (platelet factor 3) is available for coagulation protein complex formation.

This phospholipid surface forms an ideal template for the crucial concentration & orientation of these proteins for the normal coagulation cascade reactions.

Platelet fusion

High concentrations of ADP, the enzymes released during the release reaction & thrombasthenin contribute to an irreversible fusion of platelets aggregated at the site of vascular injury.

Thrombin also encourages fusion of platelets & fibrin formation reinforces the stability of the evolving platelet plug.

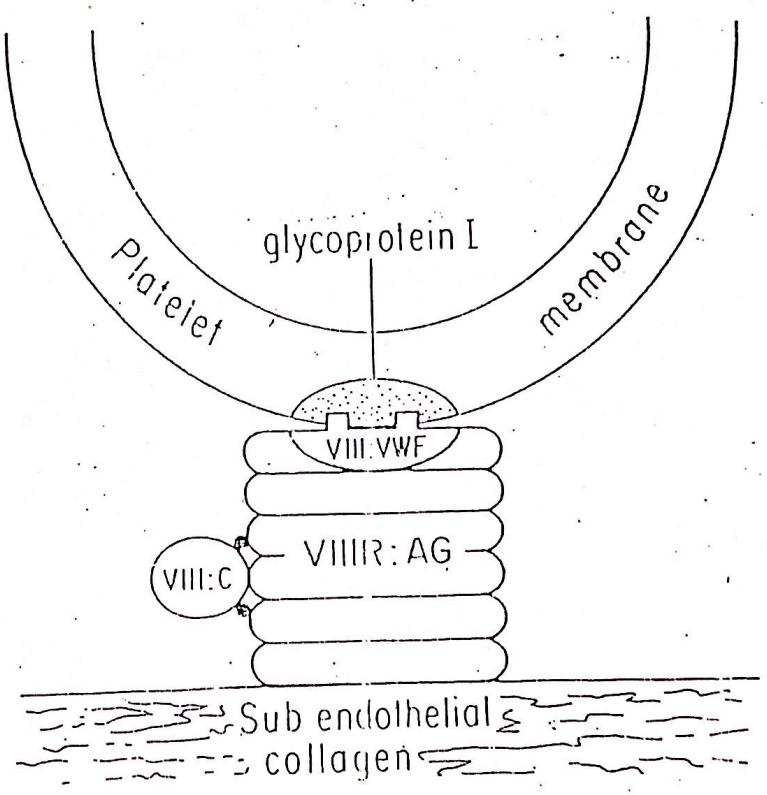


Fig. 11.3 The role of factor VIII:VWF and factor VIIIR:AG in platelet adhesion.