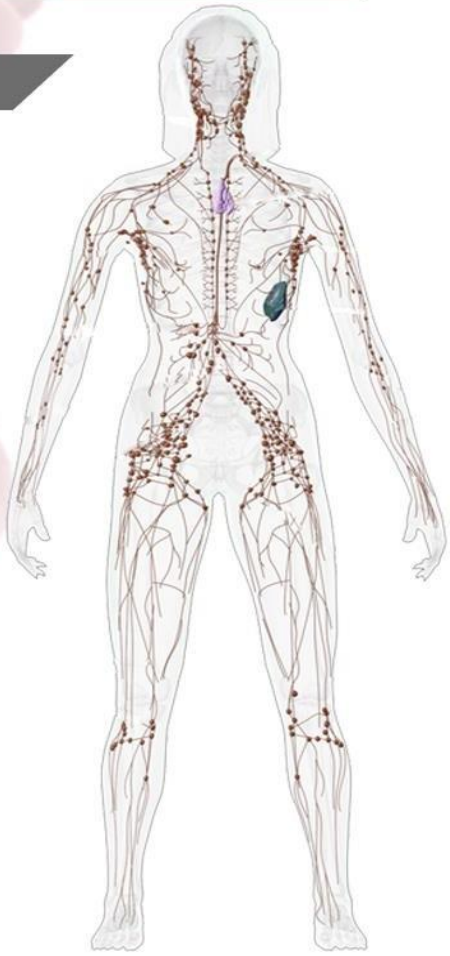
Sheet 9

Hematology and Lymphatic system

Subject | Physiology



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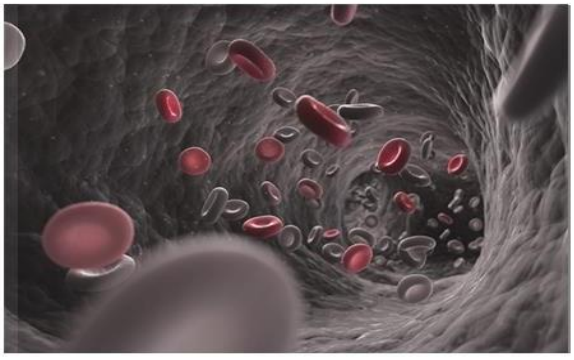


Platelets

- Platelets are developed from the giant cells called "megakaryocytes" in the bone marrow , whose diameter is usually around 100μm.A single megakaryocyte can give rise to about 4000 platelets.
- Platelets are anucleate cells, they don't contain nuclei and they are granulated bodies.
- The differentiation time from stem cell to platelet "thrombopoiesis" is about 10 days. Remember that RBCs and WBCs need 6-7 days for maturation in the bone marrow.
- Platelets production is regulated by the hormone thrombopoietin which is produced mainly in the kidney and to a lesser extent in the liver.
- Normal platelet Count is from 200,000 to 400,000/μL
- High count of platelets is called thrombocytosis → more than 450,000
- Low count of platelets is called thrombocytopenia → less than 150,000
- Platelets contain many substances stored inside their granules.
- The main function of platelets is hemostasis and blood clot formation (blood clotting).

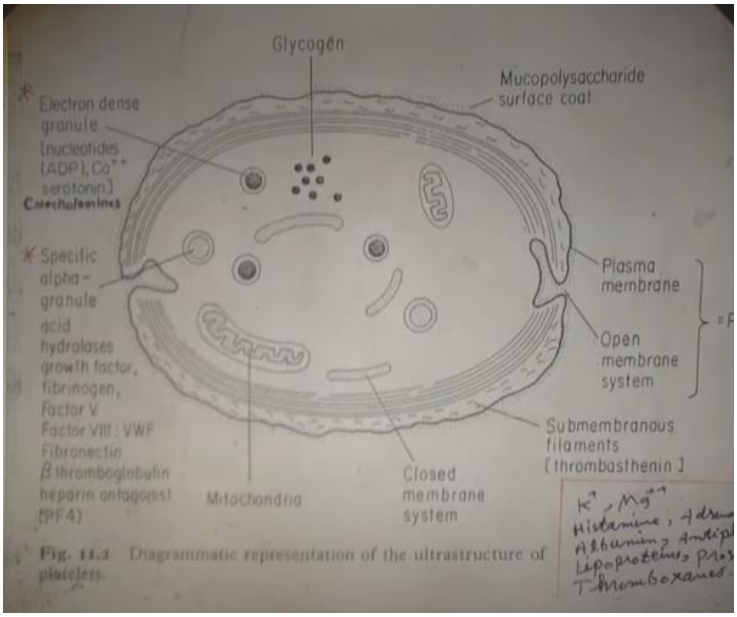
Platelets contain two types of granules:

1. **Electron dense granules:**

   Contain: nucleotides , ADP and ATP, Ca++, serotonin, and catecholamines (Adrenaline , noradrenaline , dopamine).

2. **Specific alpha granules:**

   Contain: Acid hydrolases, growth factor, fibrinogen, factors V and VIII:VWF, fibronectin, β thromboglobulin, and platelet factor-4 (a heparin antagonist).



In addition, platelets contain in their cytoplasm K+, Mg+, histamine, adrenaline, albumin, antiplasmin, glycoprotein, lipoproteins , prostaglandin, thromboxane A2.

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

Platelets maintain the integrity of blood vessels, so in the absence of platelets capillaries become weak and fragile, therefore RBCs leave the capillaries to the tissues in large numbers which is abnormal.

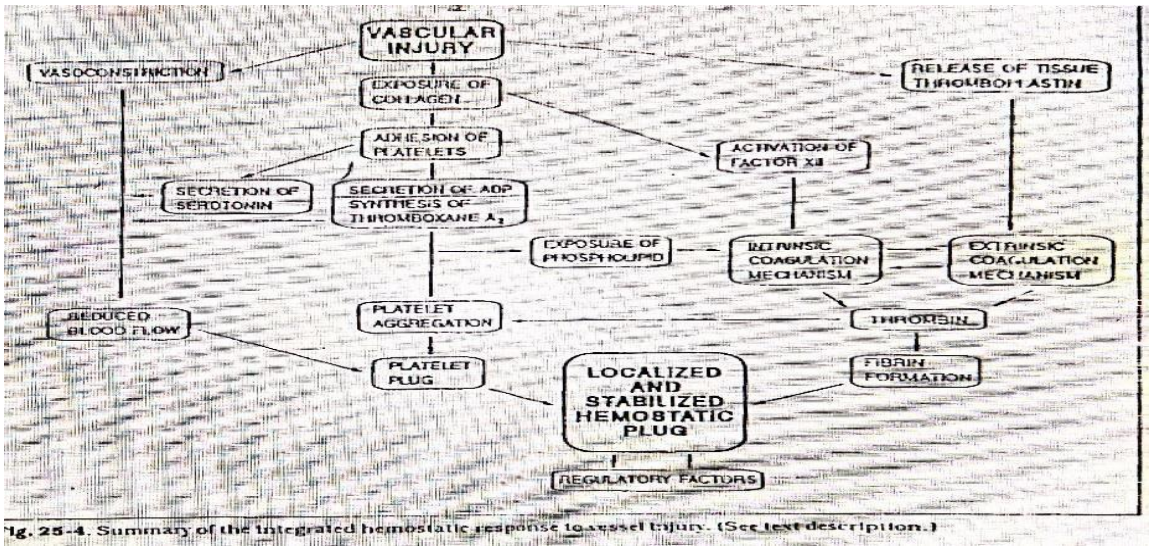


Fig. 25-4. Summary of the integrated hemostatic response to vessel injury. (See text description.)

As we said , the main function of platelets is hemostasis which means stopping bleeding from injured blood vessels

Steps of hemostasis:

1. **Vasoconstriction of the injured blood vessels**

   Factors that cause vasoconstriction:
   - Myogenic contraction (physical factor)
   - Endothelin 1 by the injured endothelial cells
   - Adrenaline
   - Serotonin (released from activated platelets)
   - Thromboxane A2

   Vasoconstriction reduces blood flow from the injured vessel.

2. **Platelet plug formation (occurs through five steps)**

A. Platelet adhesion

When the endothelial cells of the blood vessel are injured , subendothelial collagen will be exposed . Then , VWF binds to collagen , and a glycoprotein known as Gp1b on the platelet plasma membrane binds to VWF.

VWF and Gp1b are essential for platelet adhesion, and if they were genetically deficient, the patient shows increased bleeding tendency.

Two important factors are required for adhesion:

1. Factor VIII:VWF
2. Glycoprotein 1b (on platelets surfaces)

Note: Factor VIII is a protein produced from epithelial cells and platelets

Also, it is composed of several functioning parts, the most important are:

i. Factor VIII:VWF → required for normal platelet adhesion in hemostasis.
ii. Factor VIII: Ag → required for possible platelet aggregation.
iii. Factor VIII:C → refers to the coagulant portion of the molecule & represents the ability of the molecule to correct coagulation.

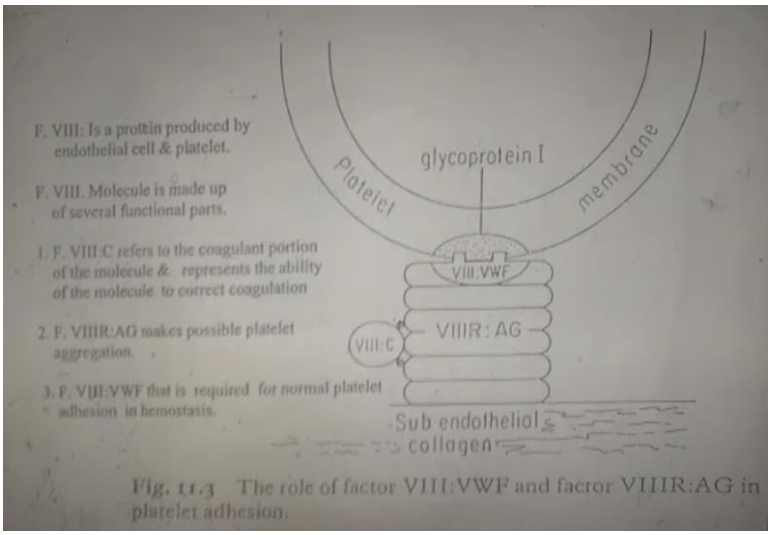


Fig. 11.3 The role of factor VIII:VWF and factor VIIIR:AG in platelet adhesion.

B. Release reaction

Adhesion causes activation and stimulation of platelets leading to the release of the content of their granules.

Activated platelets release ADP, serotonin, lysosomal enzymes and calcium ions. The most important ones are ADP and Ca++.

Activated platelets also synthesize thromboxane A2 which causes vasoconstriction as well as stimulation of platelet aggregation.

C. Platelet aggregation

The exposed collagen attracts more platelets to the injury site and many of the released granule contents including **thromboxane A2**, stimulate platelet aggregation.

At the same time of injury normal endothelium adjacent to the site of injury produces **prostacyclin PGI2** and **nitric oxide** to prevent spread of platelet aggregation to the adjacent normal areas (**prostacyclin** and **NO** inhibit platelet aggregation and vasodilate blood vessels).

The released thromboxaneA2 and ADP cause further platelets aggregation , (ADP causes membrane of other platelets to swell encouraging their aggregation).

Note: Aspirin delays or inhibits the production of thromboxane A2 , that's why some people take aspirin as a preventive medicine to decrease the formation of blood clots.

D. Platelet procoagulant activity

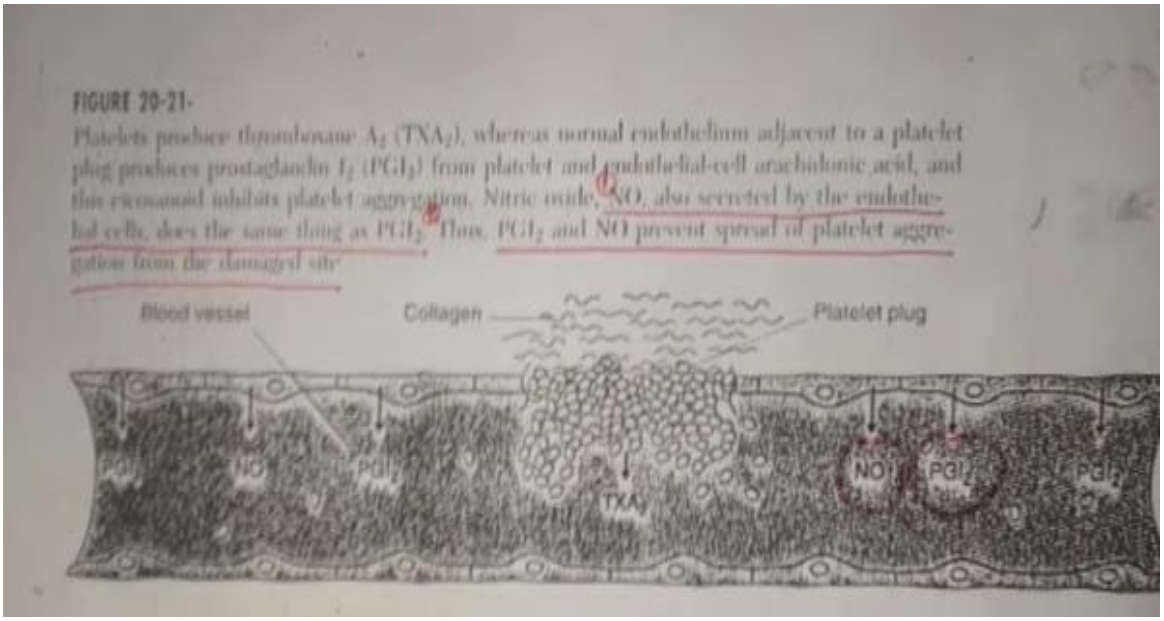
After platelet aggregation and release reaction , the exposed membrane phospholipid (platelet factor 3) is available for coagulation protein complex formation.

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

E. Platelet fusion

After vasoconstriction, platelets plug formation and clotting injury is closed.
High concentrations of **ADP** , the **enzymes released during the release reaction** and **thrombasthenin** contribute to an irreversible fusion of platelets aggregated at the site of vascular injury.

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



Extra notes

- Hemostasis is divided into two stages: **primary** and **secondary** hemostasis.
- In primary hemostasis a platelet plug is formed ,but this may be too weak or loose to seal a large cut in a blood vessel. So, secondary hemostasis exists to stabilize the weak, loose platelet plug, forming a blood clot.
- Primary Hemostasis = **Formation of a weak platelet plug**. This is mediated by interactions between the **endothelium** and **platelets**. (This sheet)
- Secondary Hemostasis = **Stabilization of the weak platelet plug**, forming a stable insoluble blood clot (**fibrin clot**). This is **mediated by the coagulation cascade**. (Next sheet)
- A blood vessels is composed of three layers, arranged from the lumen outwards as the following:
  1-Endothelium and basement membrane (contains collagen).
  2-Smooth muscles for vasodilation and vasoconstriction.
  3-Layer of connective tissue composed mainly of collagen