Hematology

Medical Committee
The University of Jordan

- Histology
- Biochemistry
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- lecture number : 5
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By: Amer ABU Shanab

PLATELETS

Characteristics:

- Platelets (sometimes called fragments) develop from giant cells called **Megakaryocytes** in the Bone Marrow.
- Platelets are similar to RBCs –they both don't have **nuclei-** but unlike RBCs, they have **granules** filled with substances.
- Their **differentiation time** (from stem cell to mature cell) is about 10 days.

Recall : RBCs and WBCs both take 6 days to differentiate, however mature WBCs remain in the bone marrow for an extra 6 days before leaving to the circulation.

- Their production is regulated by a hormone called **Thrombopoietin** produced by the kidney (with a little amount by liver) similar to Erythropoietin.
- They function for about 10 days. (Lifespan)
- Their count ranges from 200-400 thousand cell/micro liters.
  High count => thrombocytosis

  Low count=> thrombocytopenia.
- Platelets have granules which contain substances that are very important for platelet function. Other substances are also present inside the cell.
- They function in clotting or homeostasis.

Written by lara khalefa

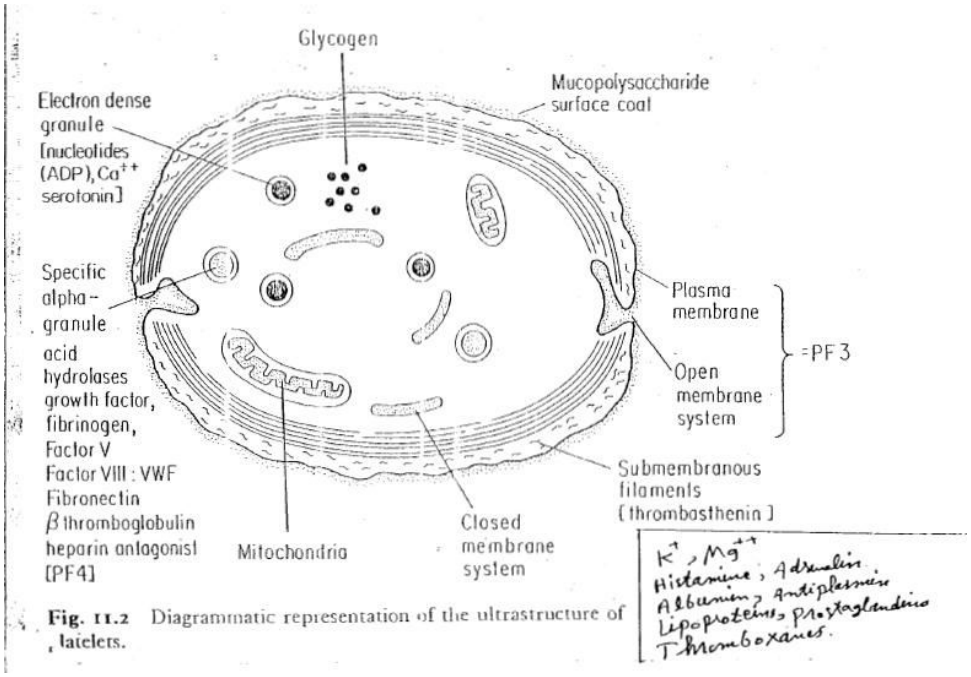

Fig. 11.2 Diagrammatic representation of the ultrastructure of platelets.

Ultra structure of platelets / what you can see inside the cell :

A- Substances such as:

potassium, magnesium, histamine, adrenaline, albumin , antiplasmine, lipoproteins, prostaglandins, thromboxanes .

B- Granules of two types:

1- Electron dense granules (Delta granules) which contain:

ATP,ADP, serotonin, calcium and chatecholamines. (Note: catecholamines are present inside the cell as well as the granules)

2- Specific /alpha granules which contain:

acid hydrolases, growth factor, fibrinogen, factor 5, factor 8, fibronectin, B-thromboglobulin, PF4 (heparin antagonist).

Note: different books tell you different things about the contents of the platelets, however the factors most important to us are mentioned in every book. (we'll take this image as an average)

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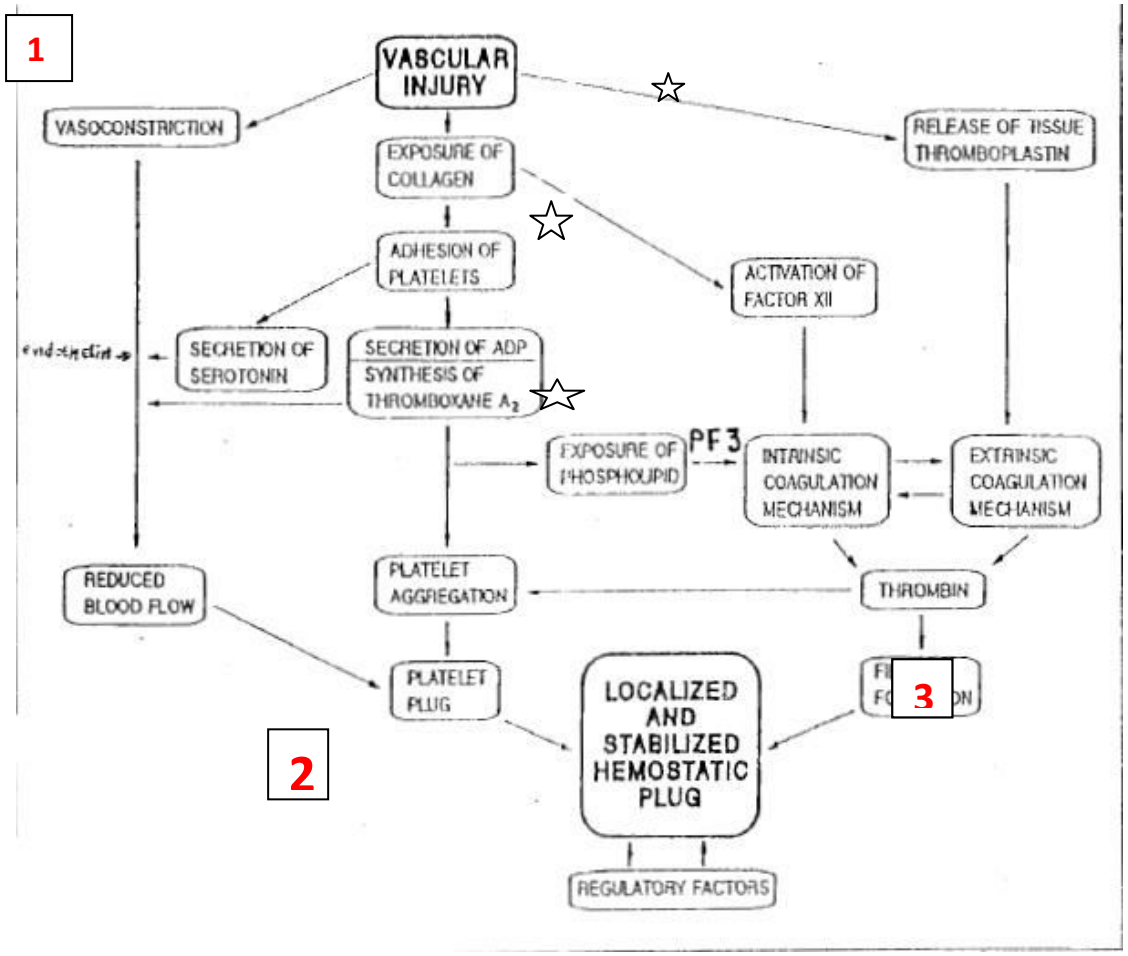
Keep in mind:

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.

- The substances in the granules are responsible for the normal integrity of blood vessels. In cases of deficiency of either the platelets or the granules inside of them, RBCs might leave the blood vessels into the tissue and this is an abnormal condition.

- Hemostasis means stopping blood loss through injured blood vessels, and this can be achieved by **three** separate processes or steps:



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1- **Vasoconstriction** via :

- Physical contraction
- Chemical factors such as: **endothelin** from the damaged cells (vasoconstrictor), **serotonin** from platelets, **adrenaline** from the granules as well as the platelets, and **thromboxane A2** from the platelets.

  All these cause **vasoconstriction** which results in **reduced blood flow.**

2- **Formation of platelet plug**

When the injury occurs to a blood vessel, platelets adhere to its surface and release substances. During formation of the plug other factors are activated or produced (star in slide) such as tissue thromboplastin, factor 12 and platelet factor 3.

3- **Coagulation/clotting mechanisms.** (we'll talk about it in upcoming lectures)

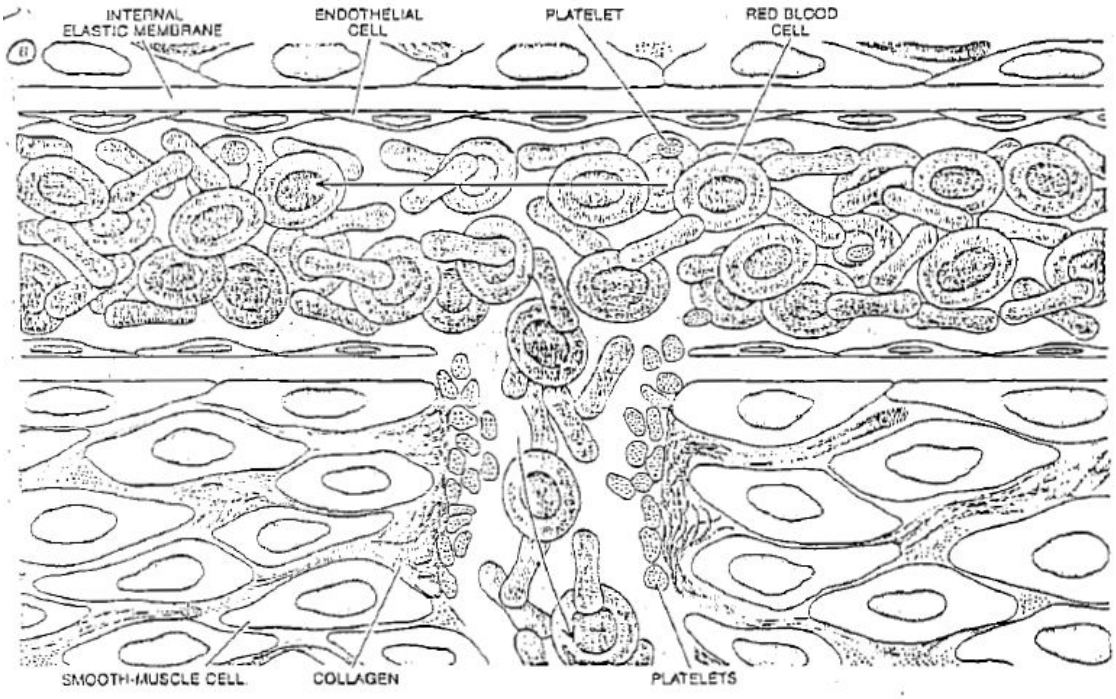
- Hemostasis is a physiological response to when a vessel is injured. If the bleeding is from a **large or medium artery** these three steps are usually **not** sufficient to stop the bleeding and other means should be resorted to (Dr Faraj mentions applying pressure as a solution).

* 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***.

Now to talk in details about the three processes:

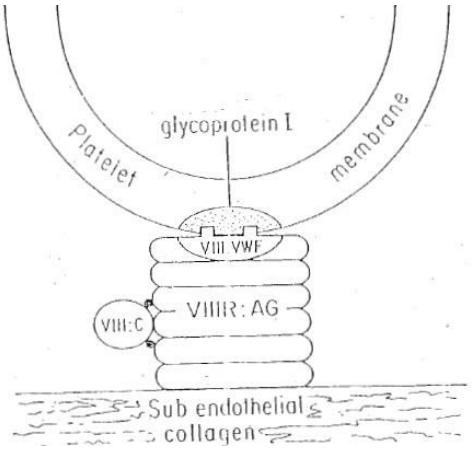


This image shows a blood vessel with blood circulating in it. When the vessel is injured, the collagen beneath the vessel's surface gets exposed and becomes sticky allowing platelets to adhere it **(1st step: platelet adhesion)**. After that the platelets get stimulated by the injured surface so they rupture releasing their substances **(2nd step: the release reaction)**. It follows that these substances from the platelets and the granules will stimulate the accumulation of the platelets above each other **(3rd step: platelet aggregation)** and then they fuse all together in their site **(4th step: Fusion).** These 4 steps lead to platelet plug formation.

*** **first step** /platelet adhesion

Very important factors are needed:

1-Glycoprotein 1 on the surface of the platelets. Sometimes this factor is deficient therefore the adhesion doesn't occur normally.



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2-factor 8: Von Willebrand (VIII:VWF)

*It is produced by the platelets and endothelium.

*And this factor consists of three parts :

1) VIII VWF for adhesion.

2)VIIIR:AG makes possible platelet aggregation.

3)VIII:C for clotting.

***** the 2nd and 3rd step** / release reaction and aggregation :

(ver important): Collagen and thrombin activate the platelet aggregation

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.

Very important

You can see that Thromboxane A2 is produced in the platelets and without it the aggregation couldn't occur or at least would be deficient. At the same time Prostacyclin (PGI2) is produced on the intact endothelium and it inhibits the spreading of the clotting to the surrounding healthy areas, as well as causing vasodilatation.

Some people take Aspirin either as medication or preventive medicine. The function of aspirin is to delay or to decrease the production of TxA2 thus decreasing platelet aggregation and reducing the chances of thrombosis. In Europe, almost all people above 45-50 years of age take aspirin and a special dose has been produced for that cause (87.5).

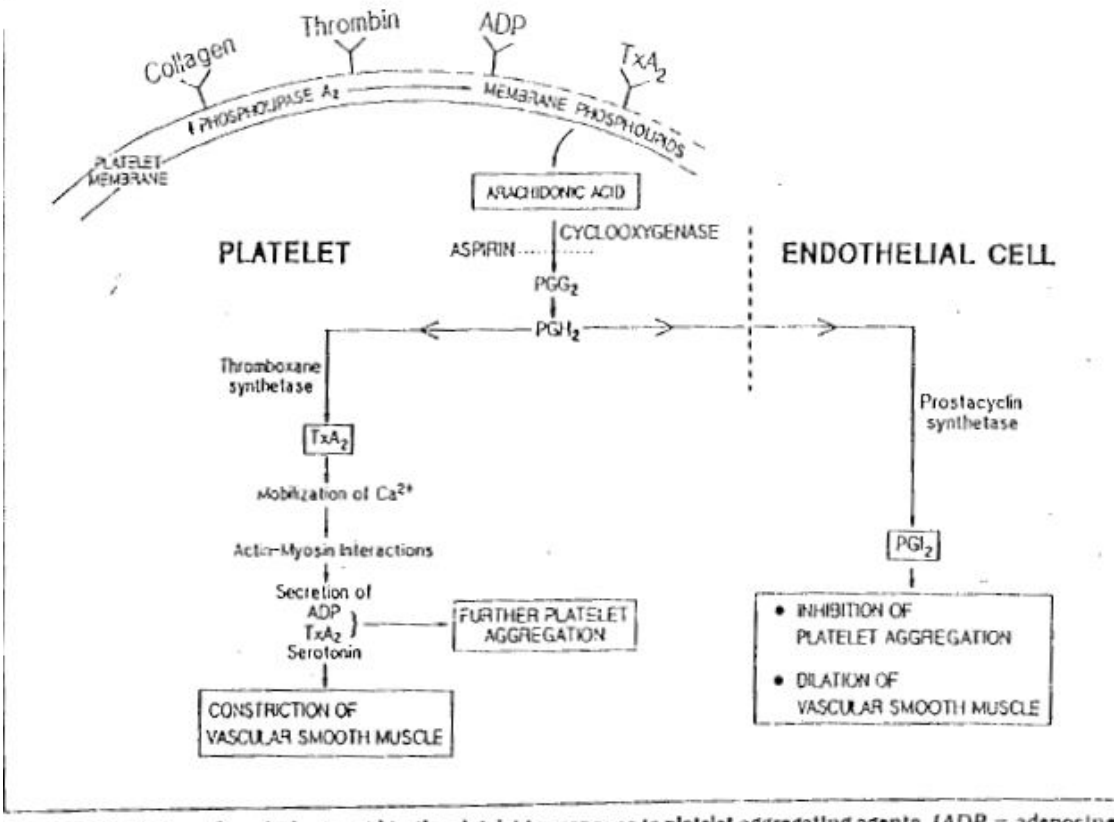

Fig. 24-3. Oxidation of arachidonic acid in the platelet in response to platelet aggregating agents. (*ADP* = adenosine diphosphate; TxA_2 = thromboxane A_2; PGG_2 and PGH_2 = cyclic endoperoxides; PGI_2 = prostacyclin.) Metabolism of arachidonate via the lipoxygenase pathway, leading to the formation of leukotrienes is not shown; its potential role in the platelet aggregation response is not clearly known. To the right of the dashed line is depicted the metabolism of endoperoxides by the endothelial cell.

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.

**now these three processes: vasoconstriction, platelet plug formation and clotting all close/fuse the injury so this is called platelet fusion .

Table 10.1 Major blood clotting factors

Factor	Name (synonyms)	Site of formation
I	Fibrinogen	Liver
II[a]	Prothrombin	Liver
III	Tissue thromboplastins	Tissue cells (membrane protein)
IV	Calcium ions	
V[b]	Labile factor	Mainly liver
VII[a]	Stable factor	Liver
VIII[b]	Anti-haemophiliac globulin A (AHG)	Platelets, RES endothelial cells, liver
vWF	von Willebrand's factor	Endothelial cells, platelets
IX[a]	Anti-haemophiliac globulin B (Christmas factor)	Liver
X[a]	Stuart factor	Liver
XI	Plasma thromboplastin antecedant factor (PTA)	Liver
XII	Hageman factor	Liver
XIII	Fibrin stabilizing factor	Liver
TF3	Platelet factor 3	Platelets

Note
[a] vitamin K-dependent [b] pro-cofactors

I asked the doctor what to memorize from this table he said" the **factor number** and its **synonyms** . Not to be asked directly about them in the exam but he might use both formulas in the exam so you need to know them to know what process he is talking about.
والله اعلم

Notes:

Factors 2, 7, 9, 10: their production needs vitamin K so they are called "vitamin K-dependent factors"

Most of these factors are produced in the **liver** so if there is a disease affecting it, such as cirrhosis, there will be an effect on the clotting mechanism.

☺بالتوفيق و ادعوا لنا بالخير