Lecture Notes

UJ | SCHOOL OF MED

PHYSIOLOGY

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019

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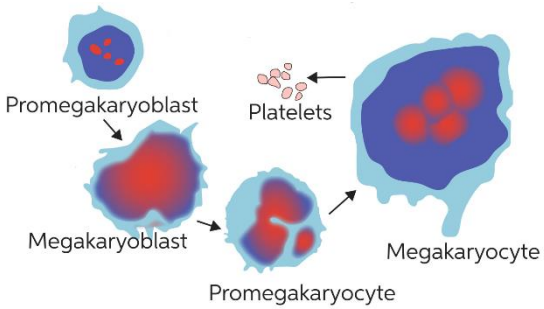
Platelets/Thrombocytes

Platelets are developed from 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' production is regulated by thrombopoietin hormone produced by the kidneys and may be a little amount produced from the liver.
Differentiation time from stem cell to platelets is about 10 days.



Platelets don't have a nucleus; they are granulated bodies.

The survival time of platelets is 7-14 days.

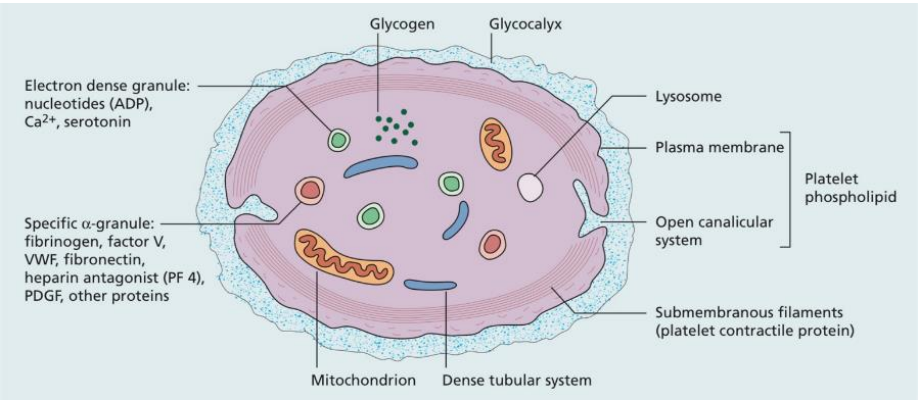
Their count ranges from 200000 – 400000 cell/µL

- Thrombocytopenia: low count (below 150000)
- Thrombocytosis: high count (above 500000)

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

Every platelet contains very important substances:

- Granules: two types of granules:
  1. **Electron dense granules**: contain ADP, ATP, calcium Ca^{+2}, serotonin, and catecholamines (adrenaline, noradrenaline, and dopamine)
  2. **Specific α granules**: contain acid hydrolysis, growth factor, fibrinogen, factor V, factor VIII, VWF (Von Willebrand factor), fibronectin, thromboglobulin, heparin antagonist (PF4 (platelet factor 4))
- The platelets also contain: K^{+}, Mg^{+2}, histamine, adrenaline, albumin, antiplasmid, lipoproteins, prostaglandin, and thromboxane A_2



Main functions of platelets:

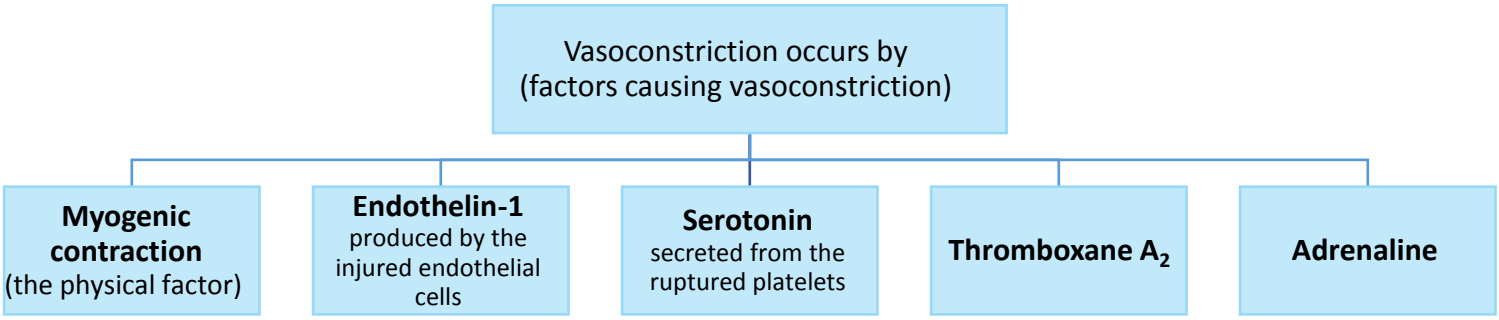
- Platelets maintain capillaries integrity and, in their absence, RBCs will leave the capillaries and will migrate through the vessel walls in large numbers
- Platelets play essential role in blood clotting.
- Platelets play a very important role in hemostasis

Hemostasis: to stop the bleeding of injured blood vessels

Stopping the bleeding of an injured blood vessel occurs through 3 processes:

1. Vasoconstriction
2. Platelet plug formation
3. Fibrin formation (cropping mechanism)

Vasoconstriction: to reduce the blood flow from the injured vessels



✓ The result: reduced blood flow

Platelet Plug Formation occurs through 5 steps:

1. Platelet Adhesion
2. Release Reaction
3. Platelet Aggregation
4. Platelet Procoagulant activity
5. Platelet Fusion

1. Platelet Adhesion

- When the blood vessel is injured, collagen is exposed, and this collagen (adhesive chemical) attracts the platelets, and because of the release of collagen and thrombin, the platelets adhere to the injured surface (the surface becomes sticky)
- In this step, two factors are important: glycoprotein 1 on the platelet membrane and factor VIII Von Willebrand factor. If these are deficient, platelet adhesion does not occur properly.

➢ ***Factor 8 (FVIII):***

FVIII is protein produced by platelets and endothelial cells
FVIII molecule is made up of several functional parts, we know three:

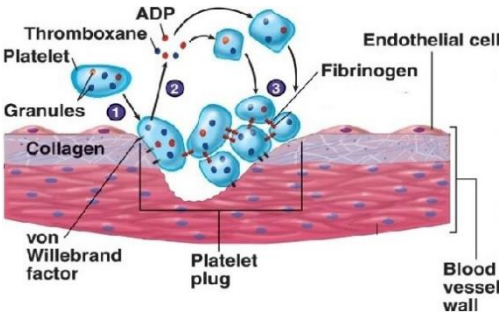
- FVIII:VWF (Von Willebrand factor) essential for normal platelet adhesion
- FVIII R:AG (factor 8 Related Antigen) essential for platelet aggregation
- FVIII:C essential for the clotting and it refers to the coagulation portion of the molecule & represents the ability of the molecule to correct coagulation

2. Release reaction

- When the platelets adhere, they are stimulated so they rapture and release their substances (thrombin, ATP, ADP, TxA_2, serotonin, fibrinogen, enzymes, heparin neutralizing factor & collagen)
- During this step, 2 main substances are produced:
  1. **Thromboxane A_2 (TxA_2)** produced by the platelets; it is essential for the aggregation, for the platelet plug formation and it's a very potent blood vessels' vasoconstrictor
     - ➢ Aspirin delays & inhibits the production of thromboxane A_2. Therefore, in people taking aspirin, there's a decrease in the amount of thromboxane decreasing the formation of thrombosis and clot formation in the blood vessels
     - ➢ If a patient takes aspirin for more than 6 months, he cannot suddenly stop aspirin & he probably should continue taking it throughout his life.
  2. **Prostacyclin I2 (PGI_2)** is produced in the endothelial cells around the injury; it inhibits the spreading of the aggregation to the surrounding area as well as it's vasodilator

Nitric Oxide (NO) is also secreted by the endothelial cells and it does the same thing as PGI_2 (they prevent the spreading of aggregation to the surrounding area)

Notice the first 3 steps



3. Platelet Aggregation

Aggregation: the platelets accumulate above each other in the injury site

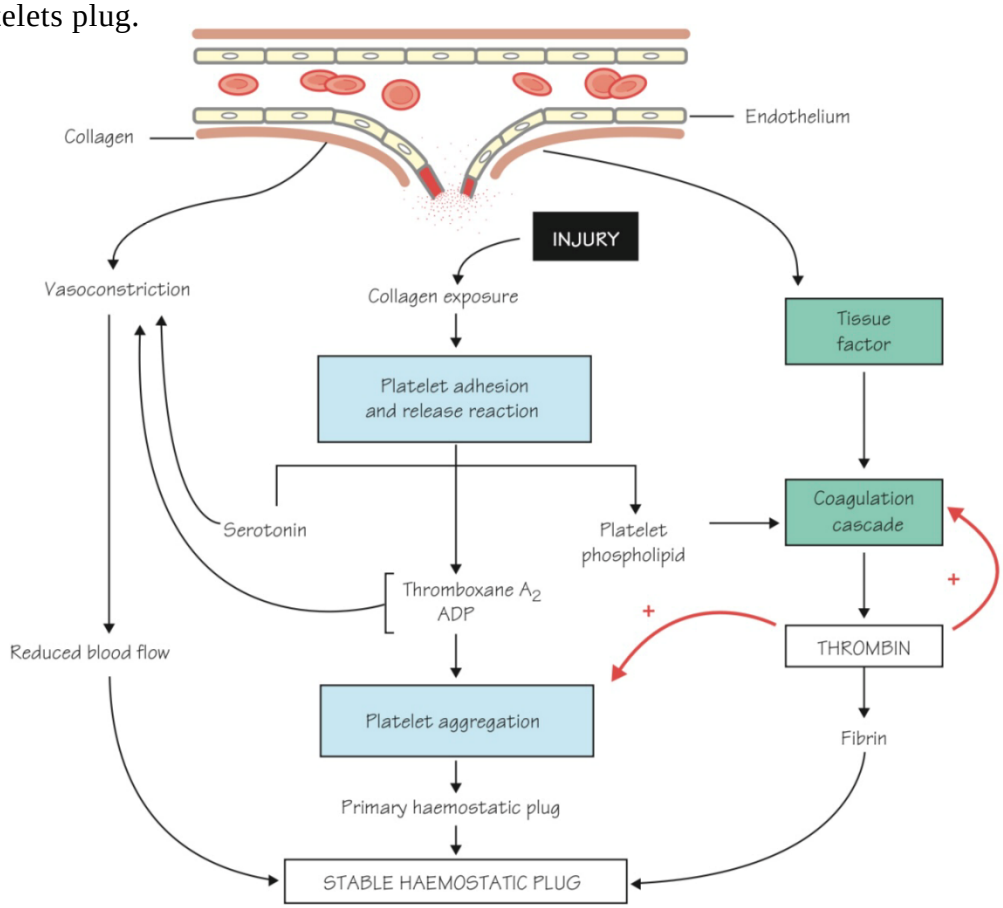
- Released ADP & thromboxane A_2 cause additional platelets to aggregate at the site of vascular injury
- ADP causes platelets to swell and encourages the platelet membrane of adjacent platelets to adhere to each other.

4. Platelet Procoagulant Activity

- When the first three steps occur one after another continuously, the medium becomes ready for the coagulation or clotting mechanism. This is called the platelet procoagulant activity
- After platelet aggregation and 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 and orientation of these proteins for the normal coagulation cascade reactions.

5. Platelet Fusion

- When that platelet plug is formed as well as the clotting mechanism, the injury is diffused
- When all these steps occur (adhesion, release, aggregation, & procoagulant), then the injury is fused and the bleeding is stopped because of the platelet plug formation
- 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 & fibrin formation reinforces the stability of the evolving platelets plug.



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