

بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ
(وَفَوْقَ كُلِّ ذِي عِلْمٍ عَلِيمٌ)



HLS Physiology | MID 6

Platelets and Hemostasis



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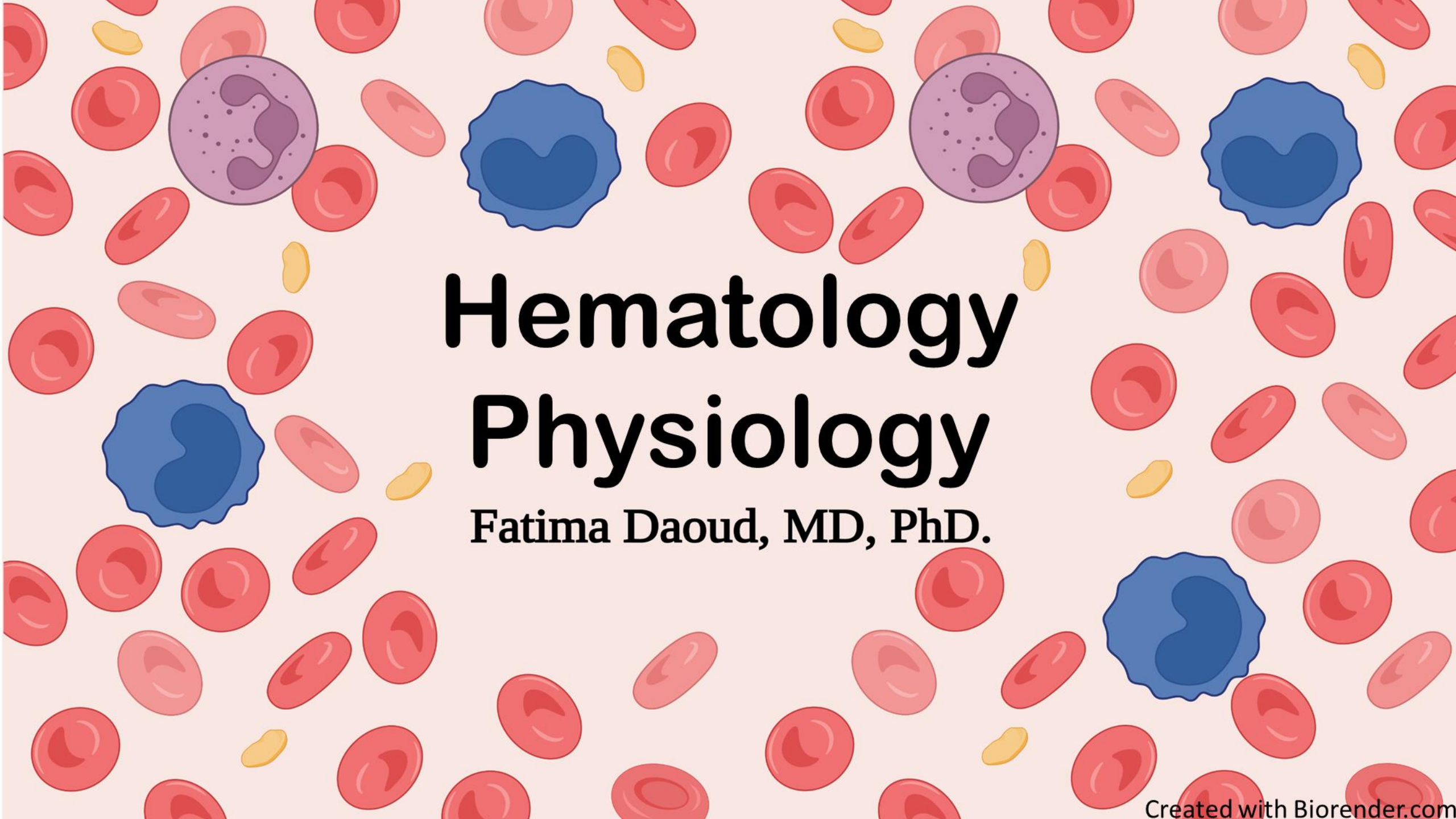
بسم الله الرحمن الرحيم،

نرجو منكم الدعاء لزميلنا في الدفعة
عون العدوان، الذي وافته المنية.

اللهم ارحمه واغفر له، وأسكنه فسيح جناتك، وأنر قبره وأنس وحشته، واجعل قبره روضةً من رياض الجنة.

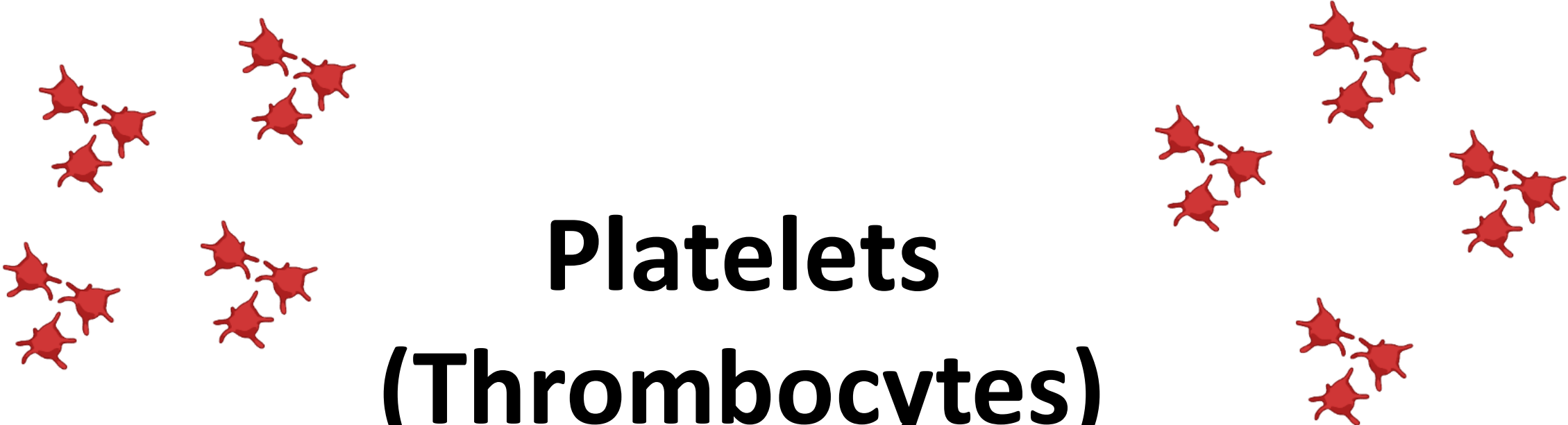
اللهم اجبر قلوب أهله وذويه، وارزقهم الصبر والسلوان، وألهمهم جميل الصبر وحسن العزاء.

رحمه الله رحمةً واسعةً وأسكنه الفردوس الأعلى من الجنة...

The background of the slide is a light pink color, populated with numerous stylized blood cells. Red blood cells are depicted as red, biconcave discs. White blood cells are shown in two types: some with a large, dark blue nucleus and a light blue cytoplasm, and others with a multi-lobed purple nucleus and a light purple cytoplasm. Small, yellow, bean-shaped cells are also scattered throughout. The text is centered in the middle of the slide.

Hematology Physiology

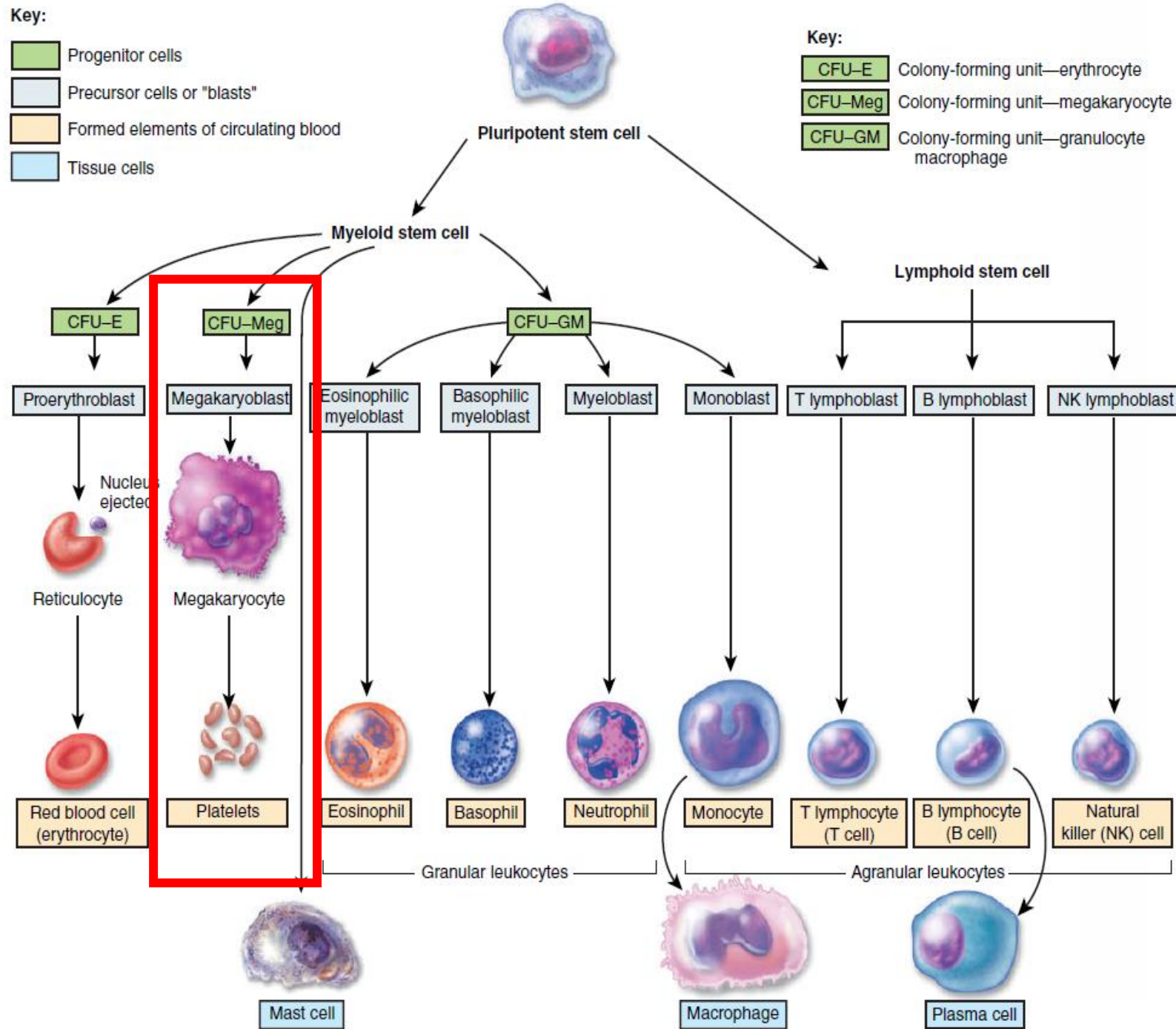
Fatima Daoud, MD, PhD.

The image features several clusters of red, star-shaped icons representing platelets, arranged around the central title. There are approximately 15-20 such icons scattered across the top half of the slide.

Platelets (Thrombocytes)

Platelets are formed in the bone marrow from megakaryocytes that originated from myeloid stem cells.

The hormone thrombopoietin, produced by the liver, increases the number of megakaryocytes in the bone marrow and induces each megakaryocyte to produce more platelets as needed.



Platelets are approximately 2-4 micrometer in size.

Megakaryocytes are extremely large, around 60 micrometer in diameter.

One megakaryocyte produces approximately 1,000 platelets. They are essentially detached vesicles containing pieces of megakaryocyte cytoplasm wrapped in plasma membrane.

Platelets are formed in the bone marrow from megakaryocytes which are extremely large cells of the hematopoietic series in the marrow.

Platelets

Overview

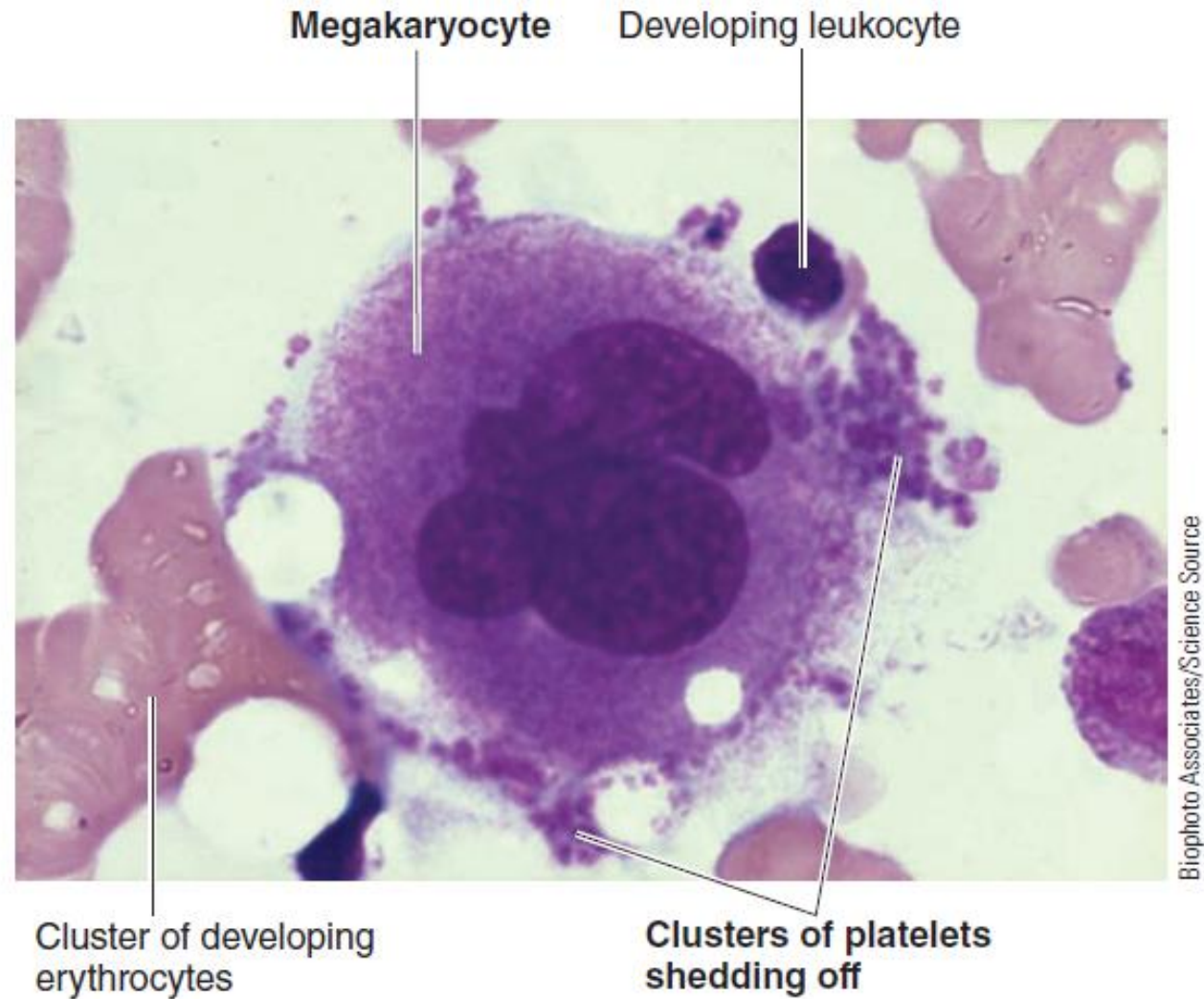
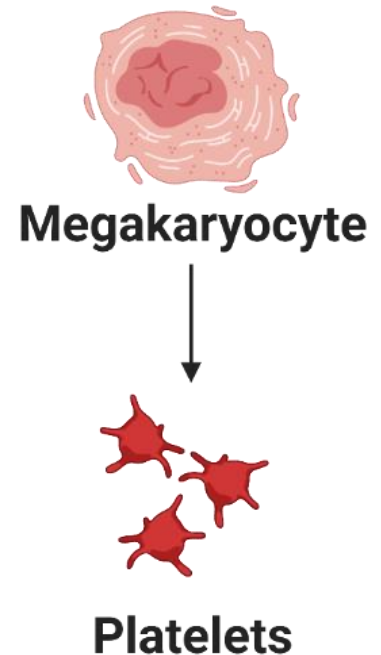


Figure 11-10 A megakaryocyte forming platelets.

Platelets

Characteristics

- The normal concentration of platelets in the blood is between 150,000 and 450,000/ μL .
- Half-life in the blood of 8 to 12 days.
- Eliminated from the circulation mainly by the tissue macrophage (Spleen **and liver**).
- **Old platelets are replaced by newly released platelets from bone marrow.**



Platelets

Cytoplasm

- They do not have nuclei. Because platelets are cell fragments, they lack nuclei.
- However, they do have organelles and cytosolic enzymes for producing energy and secretory products, which they store in many granules scattered throughout the cytoplasm.
- However they contain:
 1. Contractile proteins: actin, myosin, and thrombosthenin. present in significant quantities. Allow the platelet to contract
 2. Residuals of both the endoplasmic reticulum and the golgi apparatus to synthesize enzymes and store large quantities of Ca^{2+}
 3. Mitochondria (ATP) and also ADP is synthesized by mitochondria.
 4. Enzyme systems that synthesize prostaglandins, they cause many vascular and other local tissue reactions.
 5. Fibrin-stabilizing factor. For blood coagulation
 6. Vascular endothelial cells, vascular smooth muscle cells, and fibroblasts growth factors. Platelets also produce growth factors that cause vascular endothelial cells, vascular smooth muscle cells, and fibroblasts to multiply and grow, thus causing cellular growth that eventually aids in repairing the

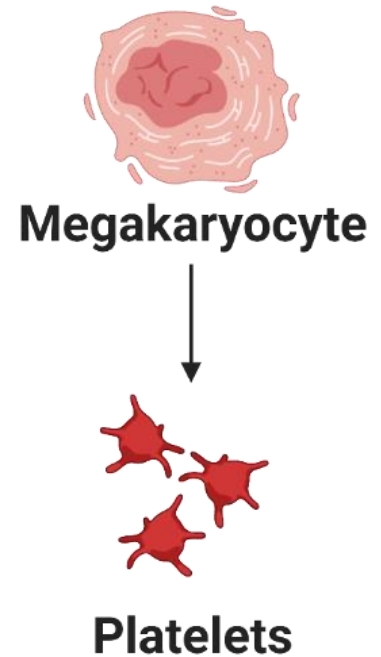


Platelets

Platelets

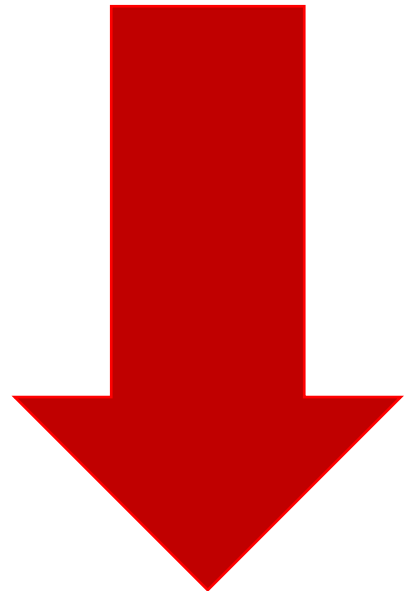
membrane

- There is a coat of glycoproteins that repulses adherence to normal endothelium and yet causes adherence to injured areas of the vessel wall. **It is directed towards injured endothelial cells and exposed collagen from deeper within the vessel wall.**
- Contains large amounts of phospholipids that activate multiple stages in the blood-clotting process.



Platelets

Thrombocytopenia



Thrombocytopenia

(Low platelets count)

So they have tendency to bleed

The bleeding mainly comes from many small venules and capillaries; causing small hemorrhages.

Normal platelet count:
150,000–450,000 / microL

<50,000/microL: increased risk of severe bleeding following surgery or injury

<10,000/ microL: spontaneous bleeding may occur.

This can also be due to abnormal platelet function

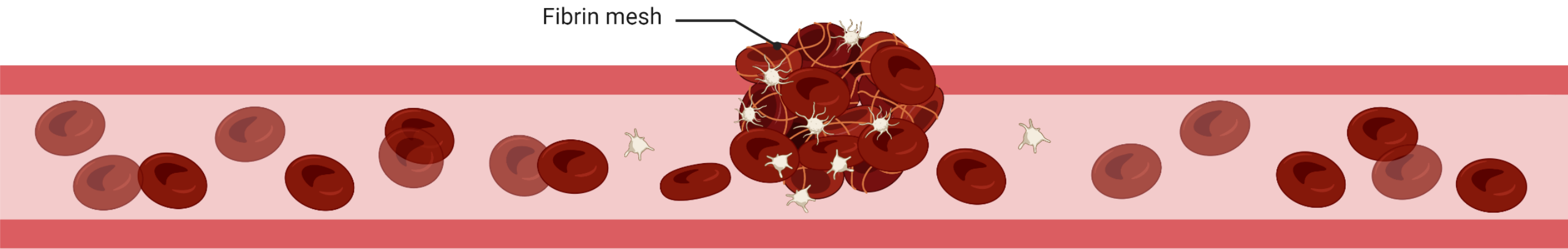
- Cutaneous and mucosal bleeding
- Easily bruising
- Petechiae
- Increased bleeding time (**bleeding time may be performed to evaluate platelet function.**)



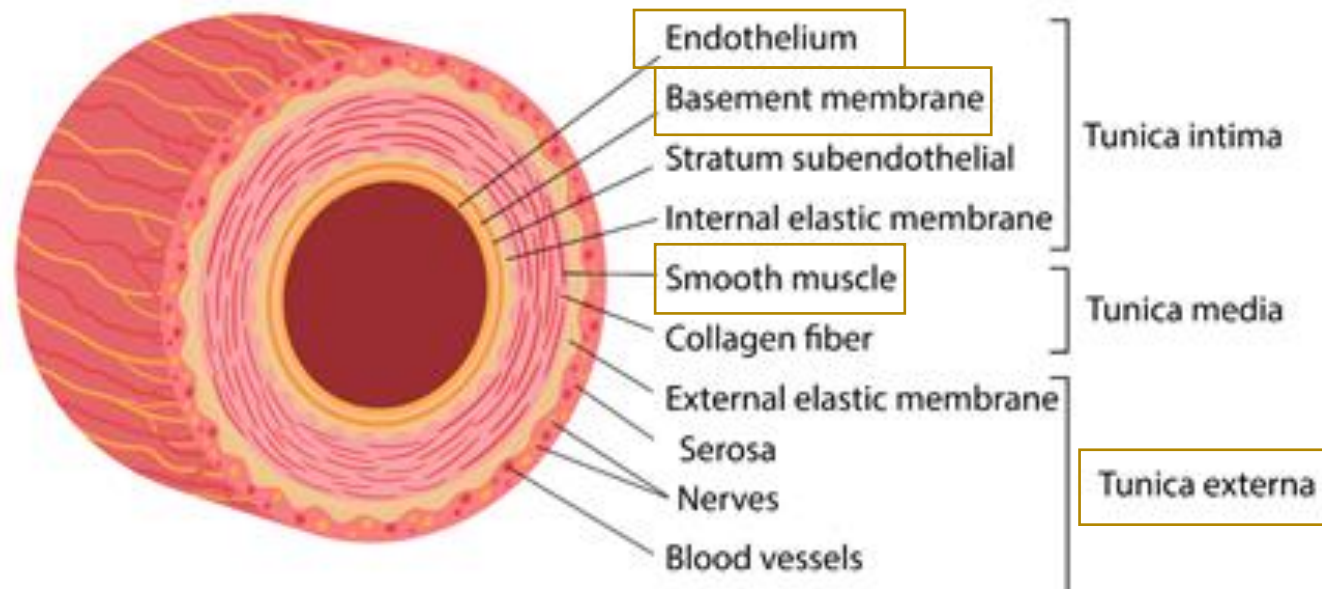
**** If the cut in the blood vessel is very small—many very small vascular holes develop throughout the body each day—the cut is often sealed by a platelet plug rather than by a blood clot.**

**** Literally thousands of small hemorrhagic areas develop each day under the skin (petechiae, which appear as purple or red dots on the skin) and throughout the internal tissues of a person who has few blood platelets. This phenomenon does not occur in persons with normal numbers of platelets.**

Hemostasis



Blood vessel anatomy



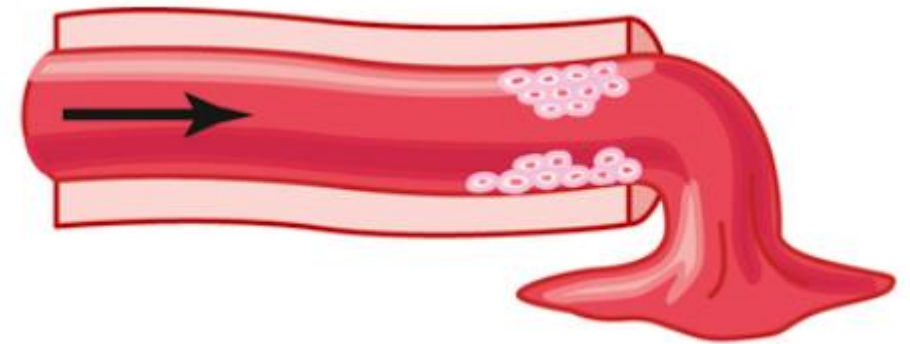
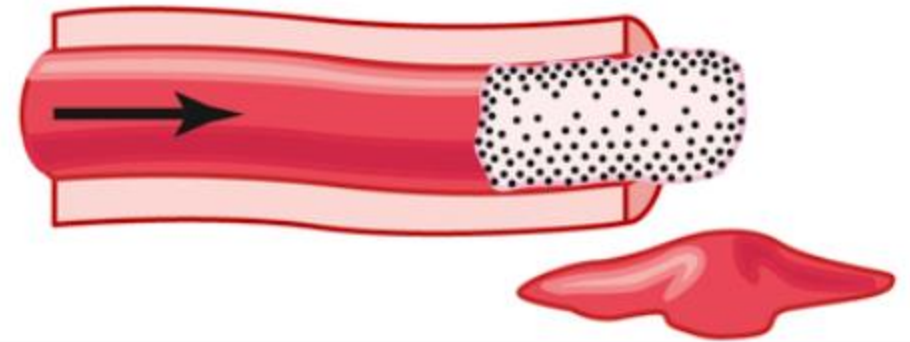
- Blood vessels are composed of 3 distinct layers:
- 1- Endothelial layer lying on basement membrane, which is primarily made of collagen.
 - 2- Smooth muscle layer.
 - 3- Outermost layer of connective tissue.

Hemostasis

Events of hemostasis

Hemostasis means prevention of blood loss and includes the following events:

- (1) Vascular constriction.
- (2) Formation of a platelet plug.
- (3) Formation of a blood clot as a result of blood coagulation.
- (4) Growth of fibrous tissue into the blood clot to close the hole in the vessel permanently.



** For bleeding to take place from a vessel, a break must be present in the vessel wall and the pressure inside must be greater than the pressure outside the vessel to force blood out through the defect.

** The small capillaries, arterioles, and venules are often ruptured by minor traumas of everyday life; such traumas are the most common source of bleeding, although we often are not even aware that any damage has taken place → The body's inherent hemostatic mechanisms normally are adequate to seal defects and stop blood loss through these small microcirculatory vessels.

** The rarer occurrence of bleeding from medium to large vessels usually cannot be stopped by hemostatic mechanisms alone. Bleeding from a severed artery is more profuse and therefore more dangerous than venous bleeding, because the outward driving pressure is greater in arteries (that is, arterial blood pressure is higher than venous pressure).

**** First aid measures for a severed artery include applying external pressure to the wound that is greater than the arterial pressure to temporarily halt bleeding until the torn vessel can be surgically closed.**

Hemorrhage from a severed vein can often be stopped simply by elevating the bleeding body part to reduce gravity's effects on pressure in the vein. If the accompanying drop in venous pressure is not enough to stop bleeding, mild external compression is usually adequate.

Hemostasis

1. Vascular constriction

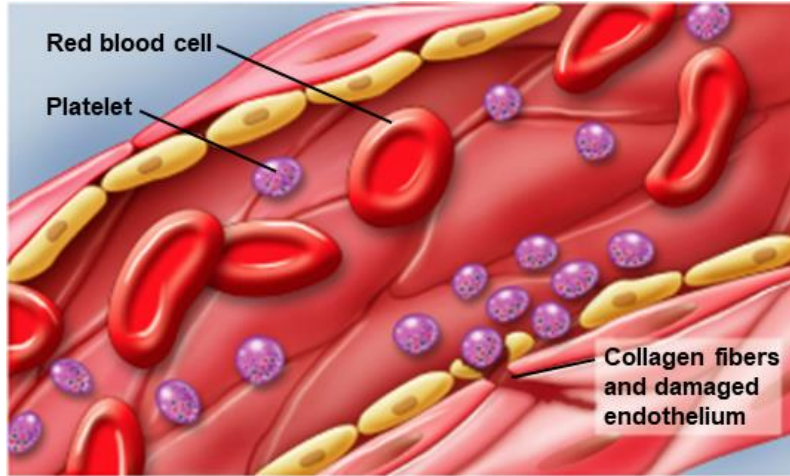
- Immediately → smooth muscle contraction.
- Reduces the flow of blood from the ruptured vessel.
- The contraction results from the following:
 - (1) local myogenic spasm**
 - (2) local autacoid factors from the traumatized tissues, vascular endothelium, and blood platelets.**
 - (3) nervous reflexes.**
- The spasm can last for many minutes or even hours, during which time the processes of platelet plugging and blood coagulation can take place.

Vascular constriction is the initial phase in the hemostasis process. Immediately after a blood vessel has been cut or ruptured, the trauma to the vessel wall causes smooth muscle in the wall to contract.

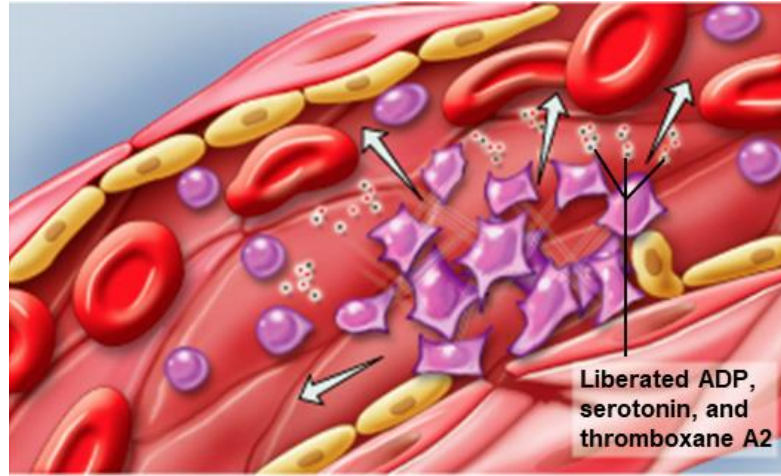
Vascular constriction alone cannot entirely stop blood loss. However, it can limit blood loss via the vessel while platelet plugging and blood coagulation processes are carried out.

Hemostasis

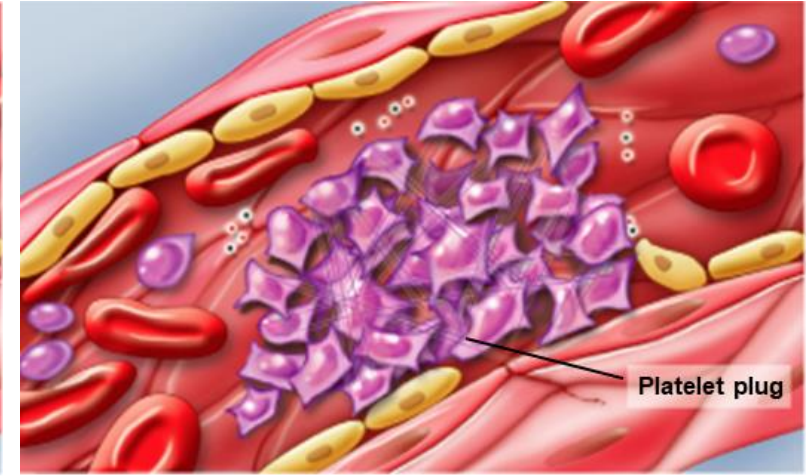
2. Platelet plug formation



1 Platelet adhesion



2 Platelet release reaction



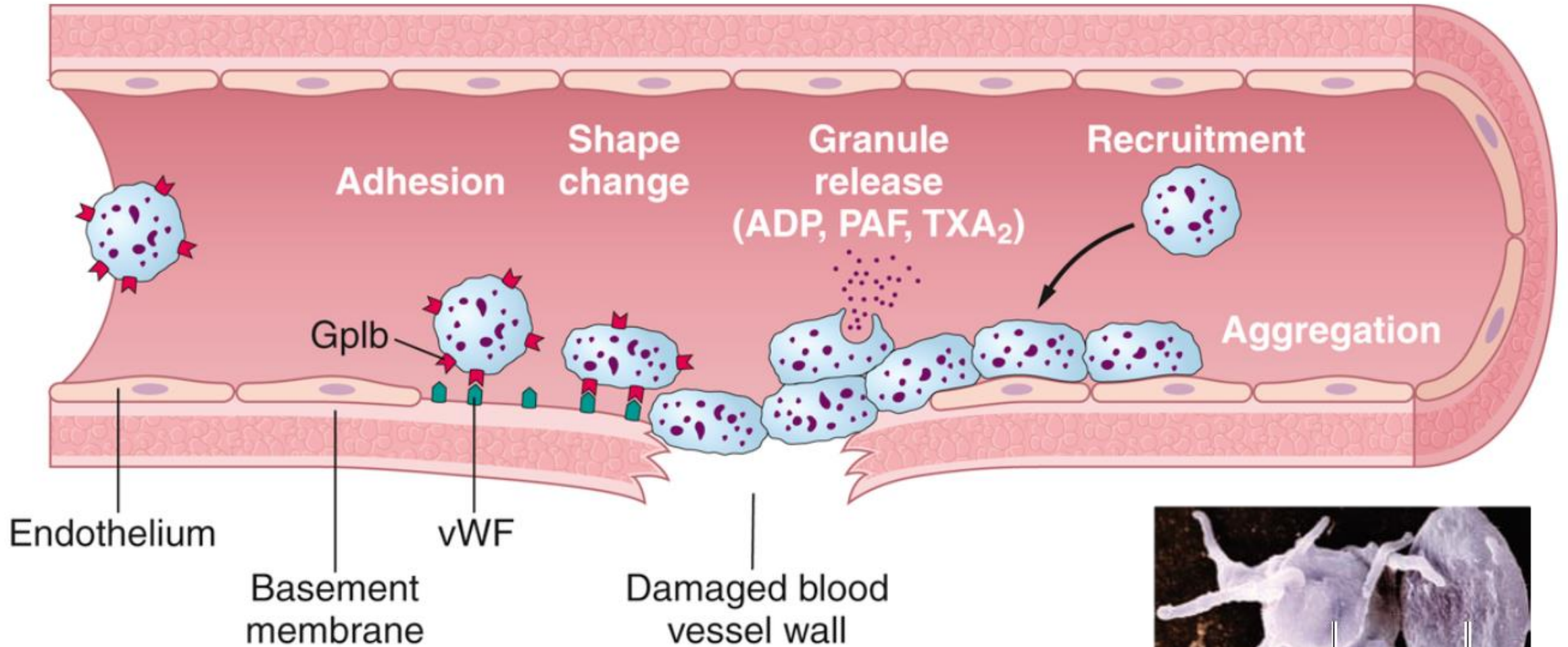
3 Platelet aggregation

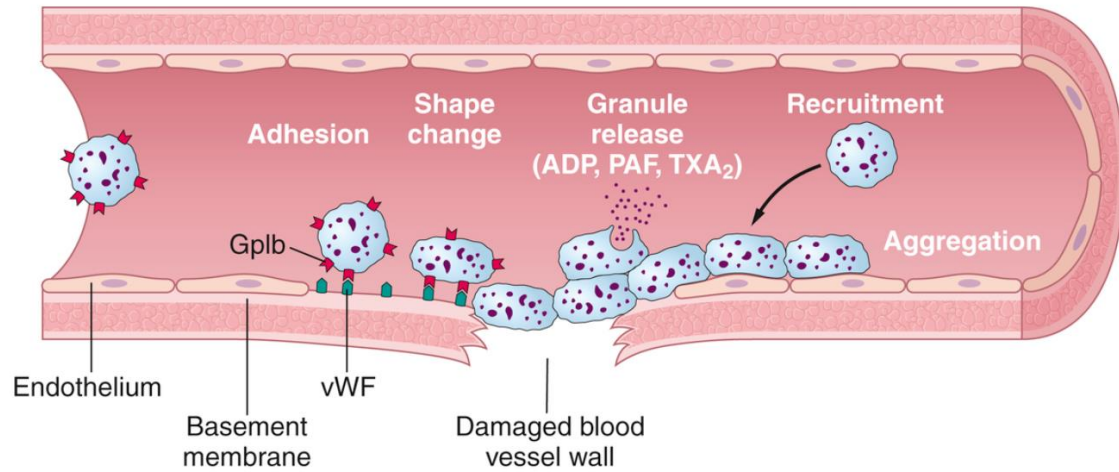
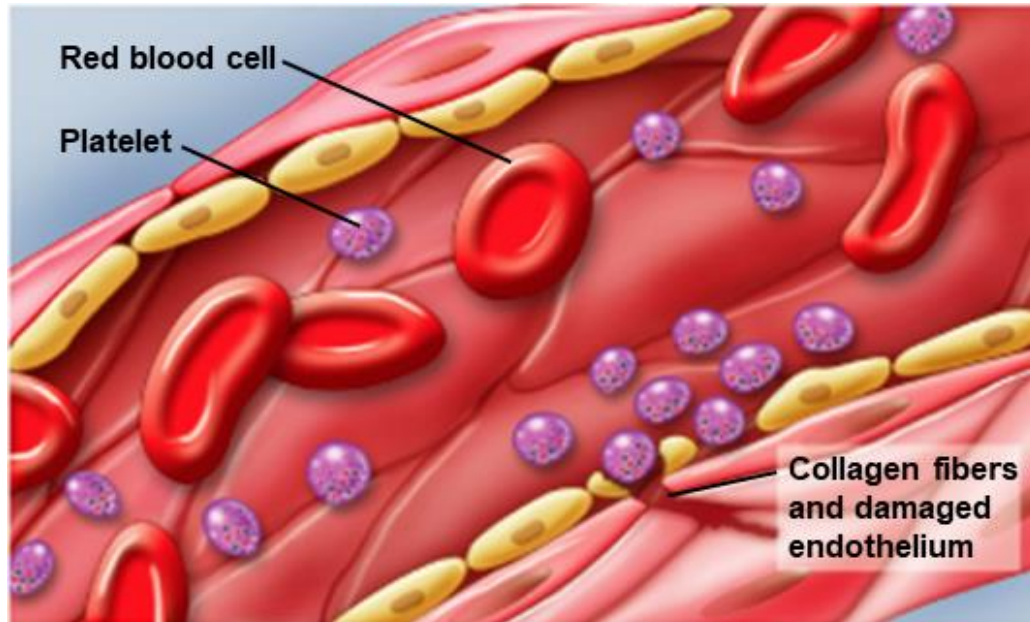
- Platelet plug formation involves three overlapping and closely linked steps. First, platelet adhesion. Second, platelet secretion or activation. Third, platelet aggregation.
- Platelets normally do not adhere to the smooth endothelial lining of blood vessels, but they do stick to damaged vessels.

- Adhesion – The deposition of platelets on the subendothelial matrix
- Secretion – The release of platelet granule proteins (Form numerous irradiating pseudopods) (They secrete large quantities of ADP and thromboxane A₂ → to activate nearby platelets.)
- Aggregation – Platelet-platelet cohesion

Hemostasis

2. Platelet plug formation





1 Platelet adhesion

1- Platelet adhesion

**** Platelets normally do not adhere to the smooth endothelial lining of blood vessels, but they do stick to damaged vessels.**

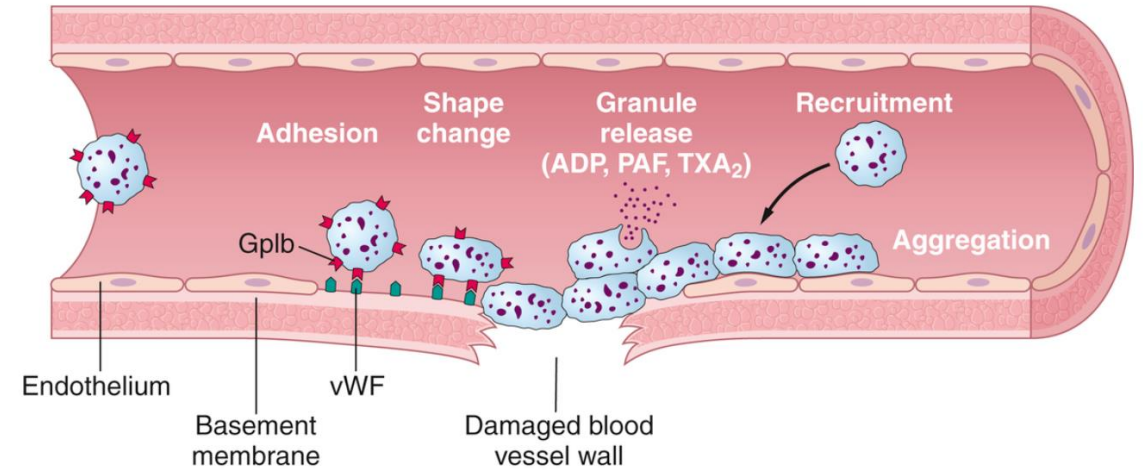
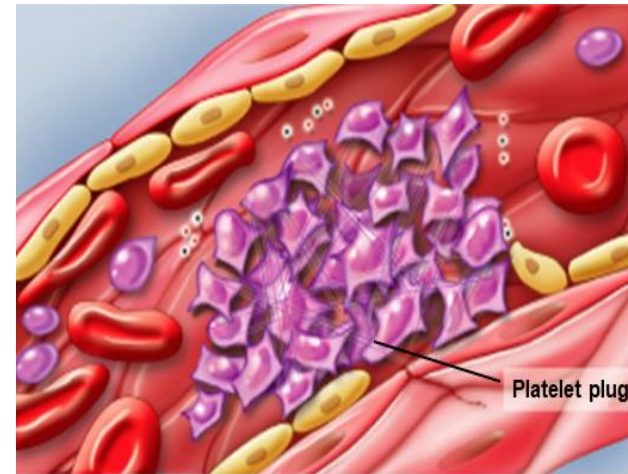
**** When the endothelial lining is disrupted because of vessel injury, *von Willebrand factor (vWF)*, a plasma protein secreted by megakaryocytes, platelets, and endothelial cells and always present in the plasma, adheres to the exposed collagen. Thus vWF serves as a bridge between platelets and the injured vessel wall**

2- Platelet secretion or activation

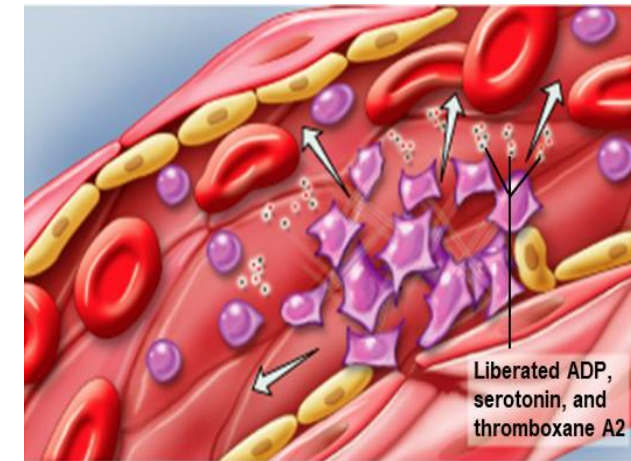
- Platelets begin to swell. They assume irregular forms with numerous irradiating pseudopods protruding from their surfaces.
- They contract forcefully, causing the release of granules containing multiple active factors, such as ADP and thromboxane A₂, which activate nearby platelets and cause vasoconstriction, respectively.

3- Platelet aggregation

- This will recruit and activate more and more platelets, which stick together or aggregate, forming finally what we call platelet plug.



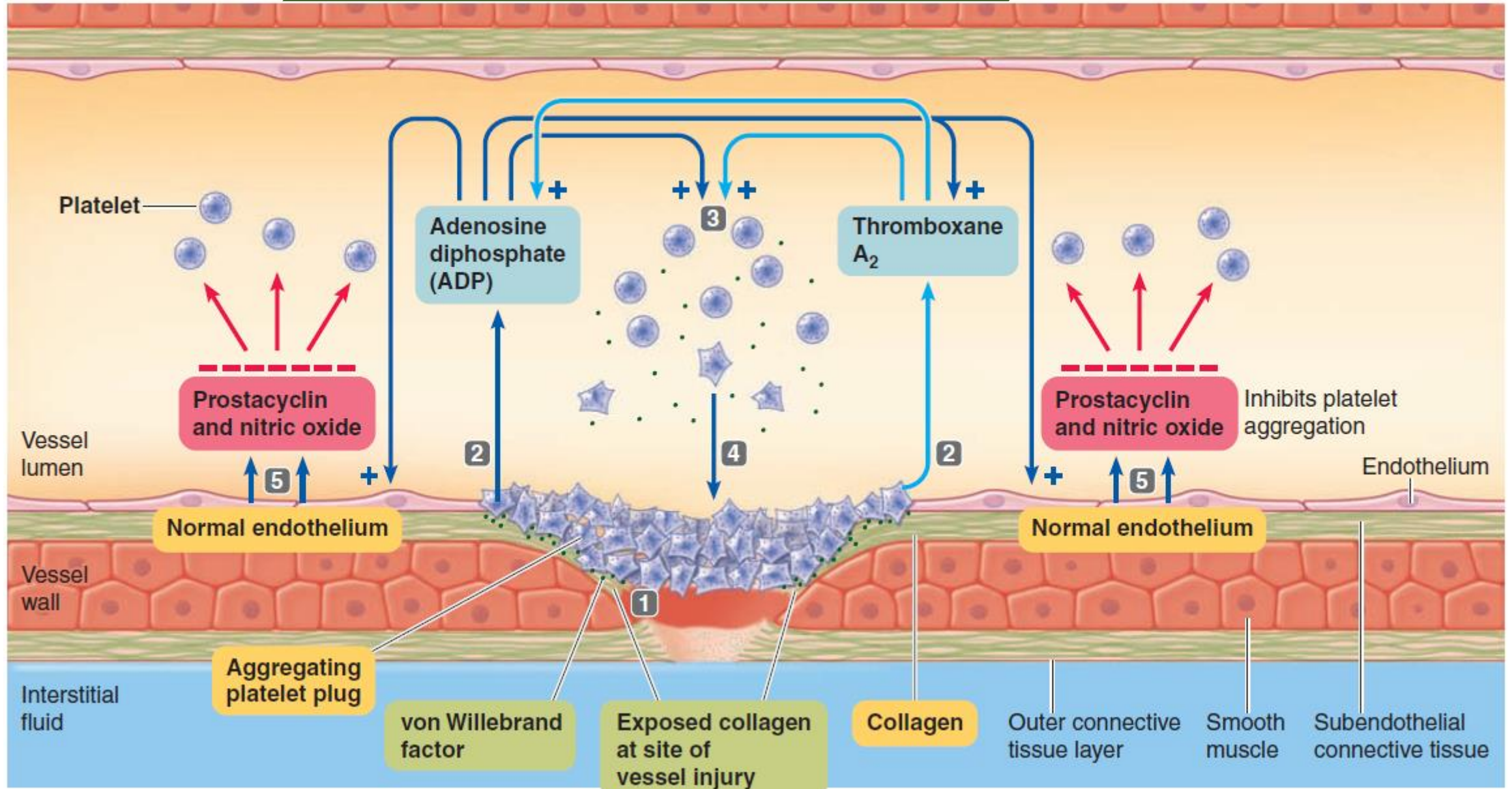
3 Platelet aggregation



2 Platelet release reaction

Hemostasis

Control of platelet plug



- Platelet-derived adenosine diphosphate (ADP) induces the adjacent intact endothelium to secrete prostacyclin and nitric oxide.
- These mediators potently inhibit platelet aggregation, thereby restricting the hemostatic plug to the vascular lesion and preventing thrombus extension across uninjured tissue.

The aggregated platelet plug not only **physically seals** the break in the vessel but also performs three other important roles:

- (1) The actin–myosin complex within the aggregated platelets **contracts** to **compact and strengthen** the plug *what was originally a fairly loose plug.*
 - (2) The platelet plug releases several powerful **vasoconstrictors** that induce **profound** constriction *of the affected vessel to reinforce the initial vascular spasm.*
 - (3) The platelet plug releases other chemicals that **enhance blood coagulation.**
- *Although the platelet plugging method is frequently sufficient to seal the innumerable minute tears in capillaries and other tiny vessels that occur on a daily basis, larger holes in these vessels necessitate the creation of a blood clot to entirely halt the bleeding*

References

1. **Hall, John, E. and Michael E. Hall. Guyton and Hall Textbook of Medical Physiology (14th Edition).**
2. Lauralee Sherwood. Human Physiology: From Cells To Systems (9th Edition).
3. Gerard J. Tortora and Bryan Derrickson. Principles Of Human Anatomy & Physiology (15th Edition)
4. Uptodate.com

رسالة من الفريق العلمي:

كَفَى بِالْمَوْتِ وَاعِظًا



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Corrections from previous versions:

Versions	Slide # and Place of Error	Before Correction	After Correction
V0 → V1			
V1 → V2			