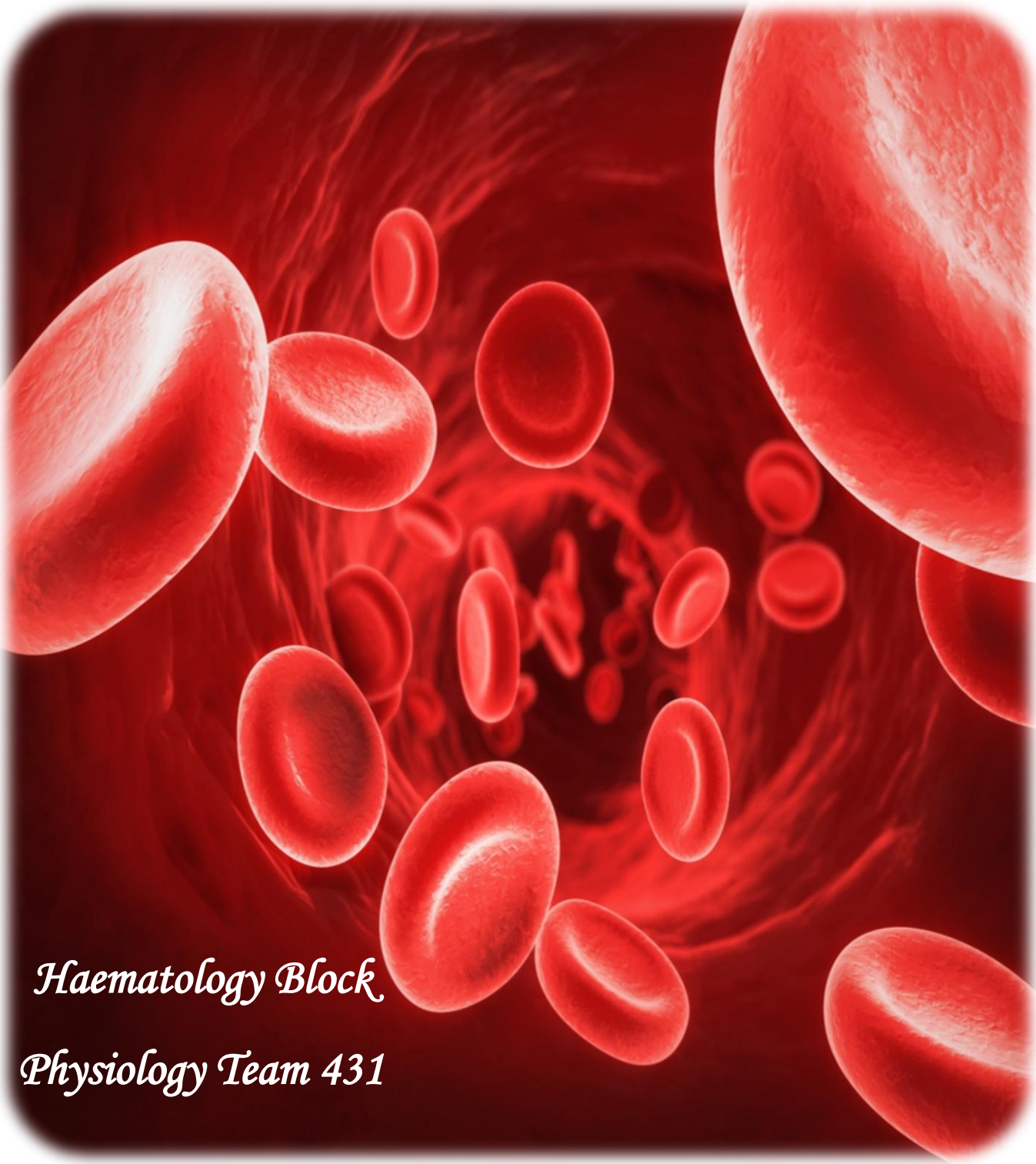


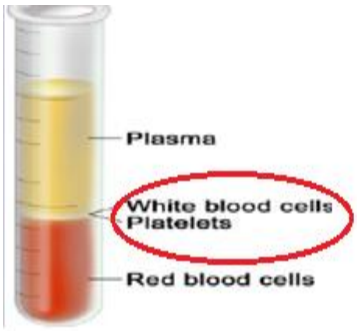
Haematology Block

Physiology Team 431

Done by : Nourah Faden

Revised by : Nour Al-Khawajah & Mohammed Asiri

Platelet Structure and Function



-What are platelets? They are the smallest cells in the blood.

- Blood: 1) Cells. 2) Plasma.
- **Buffy coat: 1) platelet 2) WBC.** ←

-Platelet (Thrombocyte):

- Anuclear and discoid cell, when it is activated it becomes spherical in shape.
- Size: 1.5 – 3.0 mm. Life span: 7 – 10 days.

-sequestered in the spleen; hypersplenism may lead to low platelet counts. (normal 150 000-450 000per microliter)

-Platelet formation (Thrombopoiesis):

Platelets are produced in the bone marrow by fragmentation of the cytoplasm of megakaryocytes. (1 megakaryocyte ⟶ 1000 platelet).
Site of formation: bone marrow.

-Steps: Stem Cell

↓

Megakaryoblast

↓

Megakaryocyte

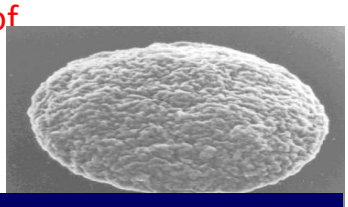
↓

Platelets

-Mature(resting) platelets: are small plate like structure. Not functioning yet, it only flows with blood.

-Regulation of thrombopoiesis: is by Thrombopoietin that comes from the liver.

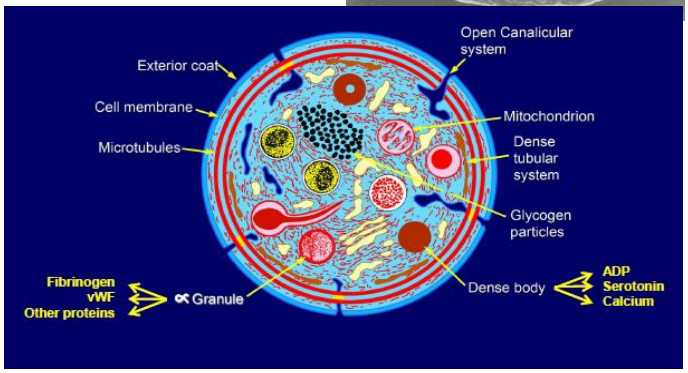
Thrombopoietin: Increases the number and maturation rate of megakaryocytes.



Surface: not smooth (looks like the brain with sulci and gyri).

-Platelet contains:

✓ Cell membrane.

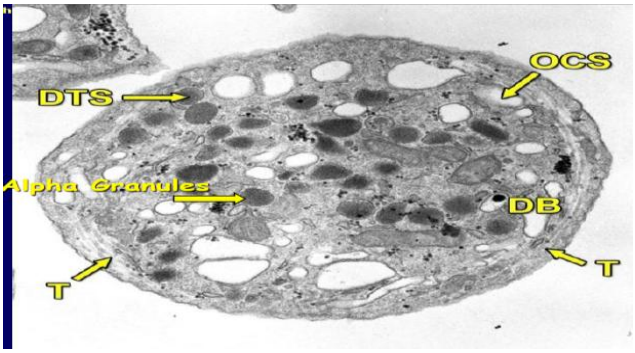


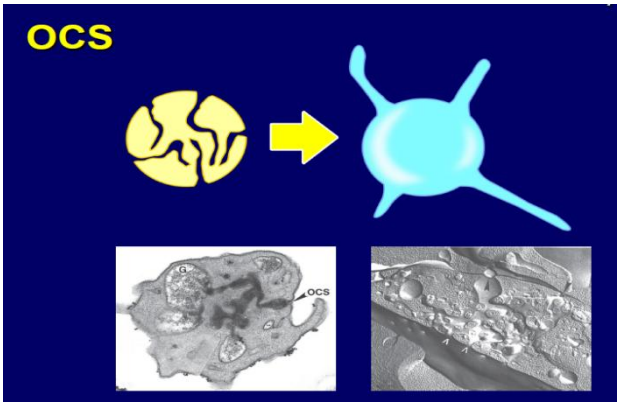
- ✓ a granules and dense body are circular, dark in color and do not have nucleus.
- ✓ Under electron microscope, a granules are more than DB.

VWF (von willebrand factor): coagulation protein produced from endothelial cells.

T: microtubules.

- ✓ Microtubules (red circles): under the cell membrane. It supports and preserves the structure of the platelet as a discoid shape.
- ✓ Glycogen particles. - Dense tubular system: stores calcium.
- ✓ Mitochondria: it means that the platelet is active.
- ✓ a granules: stores mainly protein (fibrinogen, vWF).
- ✓ Dense body DB: stores ADP, serotonin and calcium.
- ✓ The plasma membrane invaginates inside the platelet to form open canalicular system OCS (in case of resting platelet).
- ✓ Protrusions of processes in activated platelets.





-Function of OCS:

1) When platelets are activated, the content of a granules go out to the blood stream.
2) Any stimulus will get inside the through OCS.
3) Increase surface area of the platelet.

-platelet also contains other proteins:

Such as actin and myosin (in muscles for contraction), so platelets also can contract. (That's why some scientists called it the smallest muscle cell).

-Platelet receptors: imp

Receptor	Binding substance
GP Ia, GP VI	collagen
GP Ib-IX-V	vW factor
GP IIb-IIIa	Fibrinogen(circulating plasma), vW factor
P2Y12	ADP
TPα	TXA2

General function of platelets

Hemostasis: stoppage of bleeding.

1) Vascular phase: vessels constrict, blood loss decreases.
2) Platelet phase: formation of platelet plug, stop bleeding.
3) Coagulation phase: formation of fibrin clot.
4) Fibrinolytic phase: (the Dr said it's not required)

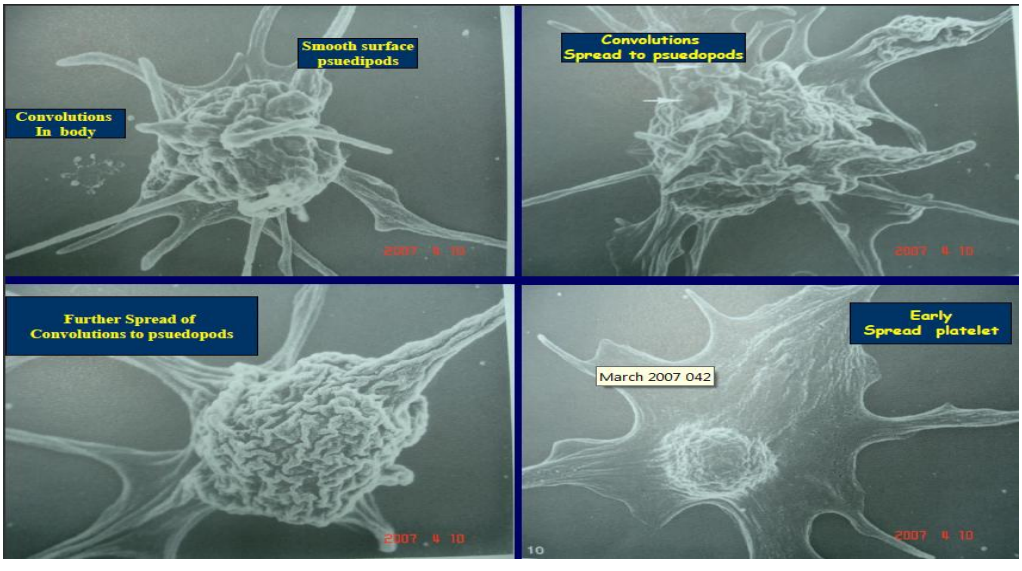
Platelet function: maintenance of vascular integrity.

1) **Initial arrest of bleeding by platelet plug formation through these steps:**
   a) Adhesion: interaction of platelets with collagen or any other surfaces except with other platelets activates platelets.

   When blood vessel is injured, the endothelial lining will be injured and the collagen (in the CT under the endothelial lining) will be exposed. Then the platelet will stick to collagen either:

   - ✓ Direct adhesion: collagen binds to platelet through the receptor GP Ia, GP VI.
   - ✓ Indirect adhesion: collagen binds to platelet through VW factor through the receptor GP Ib-IX-V.

   b) Shape change: in the resting state, platelets are discoid in shape. When they are activated, they change their shape into globular with protrusions called pseudopods.



Convolutions spread to pseudopods to increase surface area.

c) Aggregation: interaction of platelet with other platelet.

- ✓ When platelets are activated they will aggregate with each other by receptor GP IIb-IIIa, which will be activated.
- ✓ The fibrinogen in plasma will attach to these receptors leading to aggregation of platelets together.
- ✓ Fibrinogen is needed to join platelets to each other via platelet fibrinogen receptors.

d) Secretion or release reaction:

- ✓ ADP from DB: ADP is a strong chemical substance that activates nearby platelets.
- ✓ TXA2: is a prostaglandin formed from arachidonic acid Activation of membrane phospholipids

↓

Produce arachidonic acid

Cyclooxygenase ↓

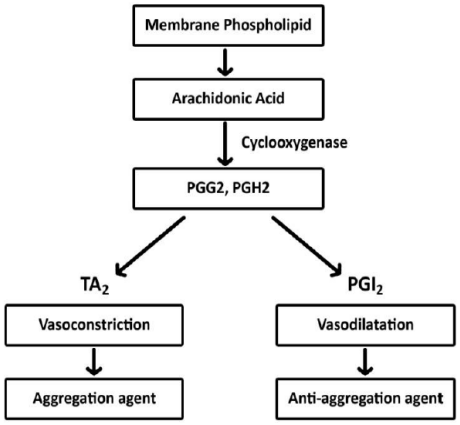
PGG2, PGH2

↓

TA2

↓

Vasoconstriction, platelet aggregation



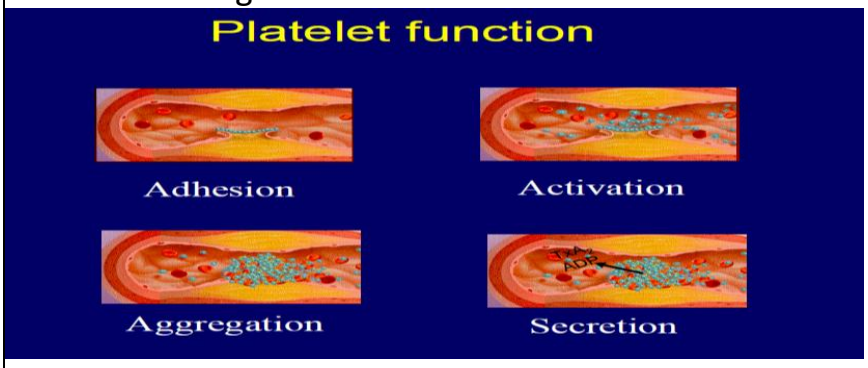
- ✓ 5HT serotonin: vasoconstriction.
- ✓ Platelet phospholipid PF3: clot formation.

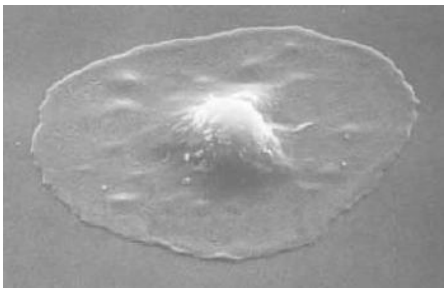
-TXA2 is inhibited by aspirin.

-Aspirin inhibits cyclooxygenase, leading to inhibition of TXA2 formation as a result prevention of clot an inhibition of platelet aggregation.

e) Clot retraction:

Myosin and actin filaments in platelets are stimulated to contract during aggregation to further reinforce the plug and help release of granule contents.





Spread platelet.

-finally primary hemostatic platelet plug is formed.

2) Stabilization of hemostatic plug by contributing to fibrin formation.

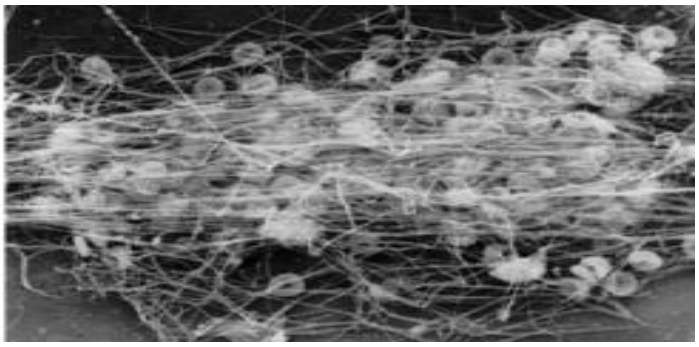
-The platelet plug formed is unstable, it needs to be stabilized by fibrin formation and this is the second function of platelets.
-Adequate number and function of platelet is essential to participate optimally in hemostasis.

Role of platelet in blood coagulation:

- ✓ Fibrin is the net result of coagulation cascade.
- ✓ Fibrin enters the primary platelet plug and stabilizes it.

What is the relation between platelet and coagulation?

When platelets are activated, the membrane phospholipid PF3 will come out and form a base or surface upon which the coagulation reactions occur.



Bleeding disorders

•Bleeding can result from:
–Platelet defects: (could lead to petechia, bruises, ecchymosis, epistaxis and prolonged bleeding)

- ✓ Deficiency in number (thrombocytopenia can be caused by bone marrow diseases (leukemia)).
- ✓ Defect in function (acquired (aspirin) or congenital).

Congenital platelet disorders:

Disorders of Adhesion:
. Bernard-Soulier
Disorder of Aggregation:
. Glanzmann thrombosthenia

Disorders of Granules:
. Grey Platelet Syndrome, Storage Pool deficiency, Hermansky-Pudlak syndrome, Chediak-Higashi syndrome
Disorders of Cytoskeleton:
. Wiskott-Aldrich syndrome
Disorders of Primary Secretion:
. Receptor defects (TXA2, collagen ADP, epinephrine)
Disorders of Production:
. Congenital amegakaryocytic thrombocytopenia, MYH9 related disorder, Thrombocytopenia with absent radii (TAR), Paris-Trousseau/Jacobsen.

1) Bernard-soulier syndrome:
Absence of GP Ib-IX-V receptor leading to problem in adhesion.
Platelet cannot function and bleeding will occur.
2) Glanzmann thrombosthenia:
Absence of GP IIb-IIIa receptor (responsible for aggregation).

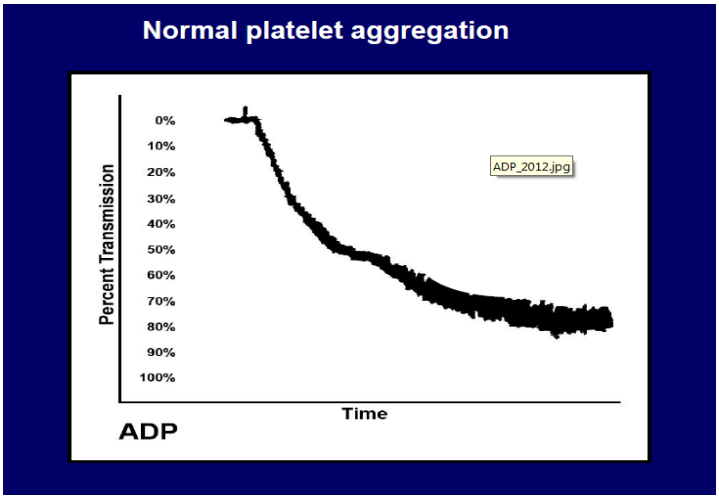
Platelet function tests

1) Platelet count and shape: if it's normal, high or low.
2) Bleeding time:
If count is normal but bleeding time is abnormal, it could be platelet abnormal function (acquired or congenital).
3) Electron microscopy: to see the organelles.
Some patients don't have a granule or they have problem in DB.
4) Platelet function analyzer (PFA:100): like bleeding time.
5) Flow cytometry.
6) Granule release product.

PRP: platelet rich plasma.

7) Platelet aggregation: this test is performed by platelet aggregometry.
-It provides information on time course of platelet activation.
-Agonists :(chemical substances that produce platelet aggregation).
ADP, Adrenaline, Collagen, Arachidonicacid, Ristocetin,Thrombin.
-Reference ranges need to be determined for each agonist (+Dose responses)
-It measures platelet aggregation by centrifuging of blood sample to separate RBCs from plasma (PRP).
-Put the tube (containing PRP) in the platelet aggregometry and add the chemical substance (agonist) to the test tube to produce platelet aggregation.

- The platelet aggregometry depends on the measurement of light transmission.
  -test tube (platelets are diffuse, resting and inactive: light will not pass.
  -test tube + ADP9aggregation forming a clot): light will pass.



Time -> Aggregation -> Light transmission

Summary

Platelet Activation-summary

- Platelets are activated when brought into contact with collagen exposed when the endothelial blood vessel lining is damaged.
- Activated platelets release a number of different coagulation and platelet activating factors.
- Transport of negatively charged phospholipidsto the platelet surface; provide a catalytic surface for coagulation cascade to occur.
- Platelets adhesion receptors (integrins): Platelets adhere to each other via adhesion receptors forming a hemostatic plug with fibrin.
- Myosin and actin filaments in platelets are stimulated to contract during aggregation further reinforcing the plug and help release of granule contents.
- GPIIb/IIIa: the most common platelet adhesion receptor for fibrinogen and von Willebrand factor (vWF).

Summary:

- Platelets are cell fragments derived from megakaryocyte in the bone marrow.
- Platelets play a pivotal role in haemostasis by arresting bleeding from injured blood vessels.
- Bleeding can result from: Platelet defects
- Acquired or congenital.

Questions

1- Regarding platelet aggregation:

A. Platelets interaction with each other
B. Release of ADP
C. Formation of fibrin clot
D. They interact with the vessel wall

2- The regulation of Platelet production is by:

A. Thrombin
B. Thrombopoietin
C. Fibrin
D. Plasmin

3- The major source of platelets contents

A. Open canalicular system
B. Alpha And dense granules.
C. Mitochondria.
D. Microtubule.

4- which of the following is receptor for collagen

A. GP Ib receptor
B. GP V receptor
C. GP IIb receptor
D. GP VI receptor

5- which of the following receptor is activated in aggregation step

A. GP Ib receptor
B. GP Ib-IIIa receptor
C. GP IIb-IIIa receptor
D. GP VII receptor

Answers

1- A
2- B
3- B
4- D
5- C