Physiology Team

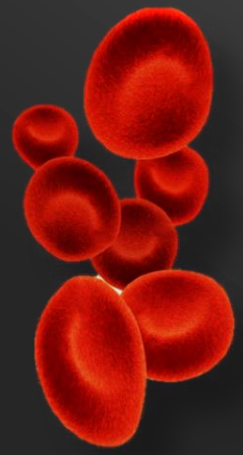
LECTURE 2

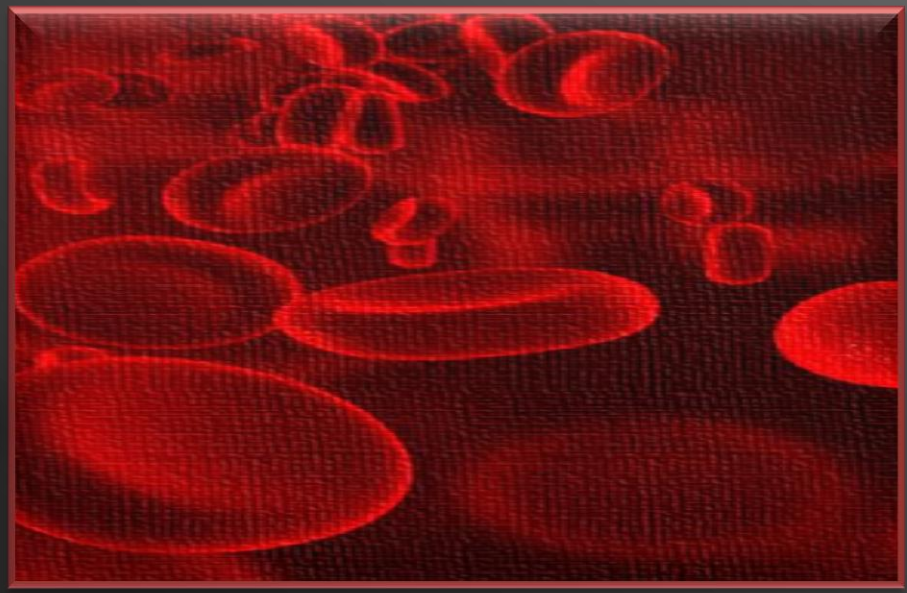
Platelet Structure & Function

HAEMATOLOGY BLOCK

DONE BY:
Eman AlBediea

REVISED BY:
Mohammed Jameel





OBJECTIVES

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At the end of this lecture, student should be able to describe:

- Understand platelet normal ultrastructure.
- Understand the functions of different platelets organelles and surface receptors.
- Understand the mechanisms of platelet functions.
- Relate membrane receptors and granule content to normal function in hemostasis and bleeding (platelet) disorders.

MIND MAP

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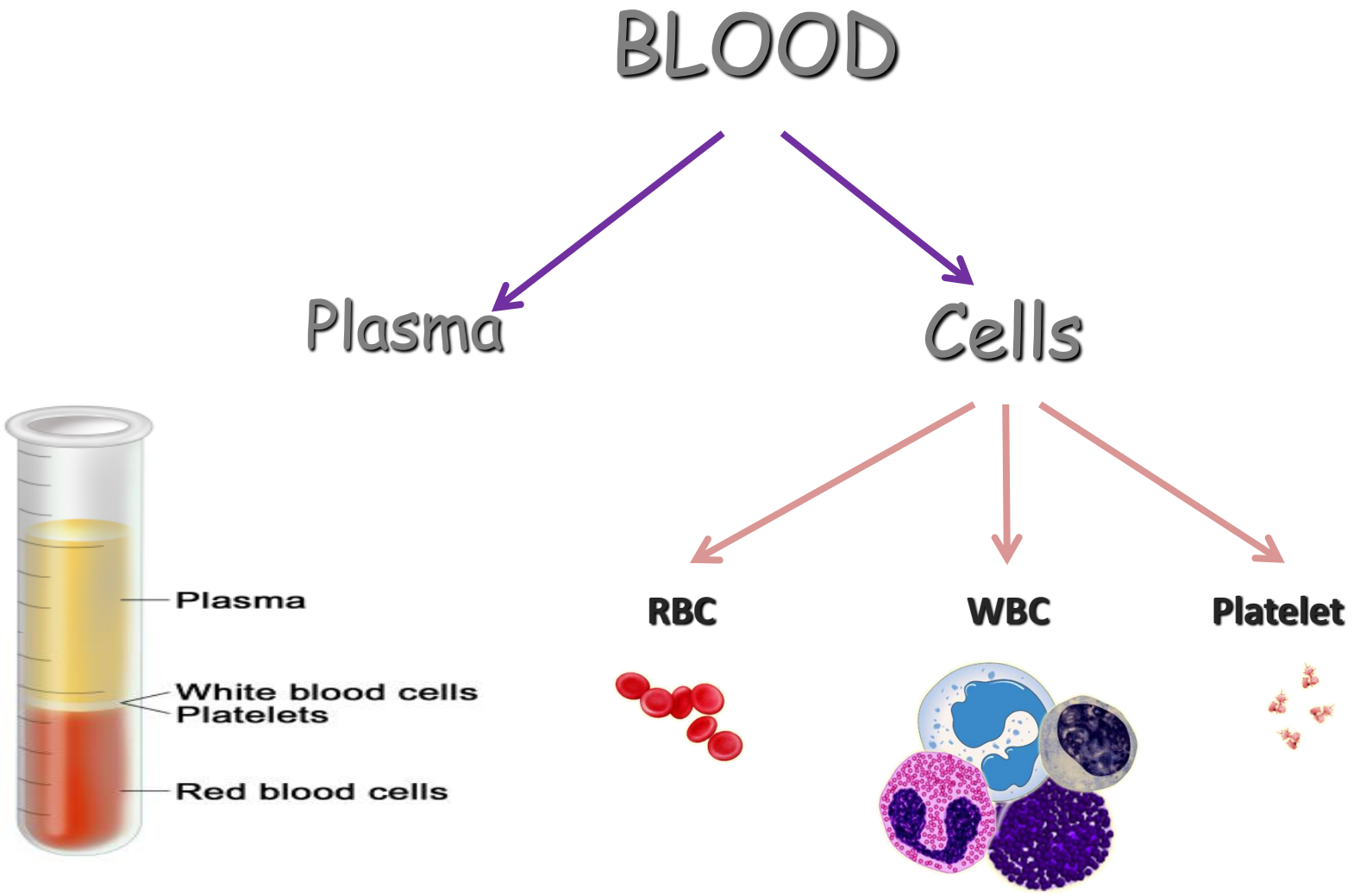
- Platelet normal ultrastructure
- Functions of different platelets organelles and surface receptors
- The mechanisms of platelet functions
- Platelet membrane receptors and bleeding (platelet) disorders

What are platelets?



■ Slides ■ Important ■ Females' Notes ■ Explanation ■ Males' Notes

What are platelets?

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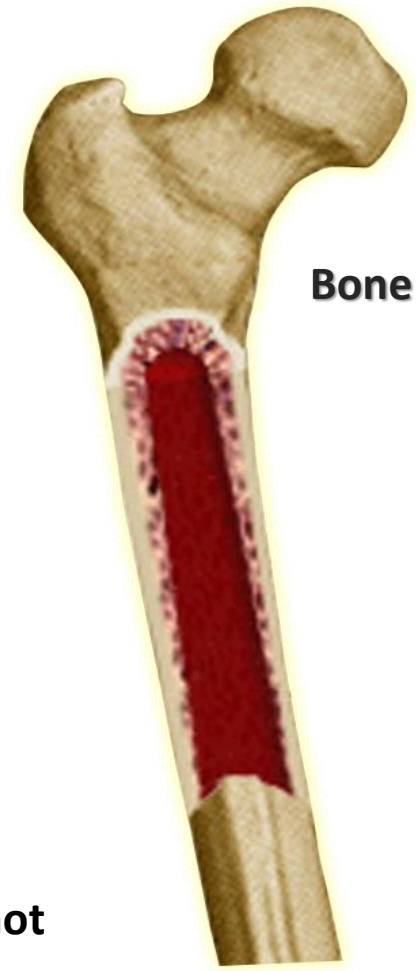
Site of formation:

- Bone marrow

Steps:

Stem cell → Megakaryoblast → Megakaryocyte → platelets

Megakaryocyte contains the platelets .
When the platelets become mature the megakaryocyte breakdown and release the platelets into the circulation .



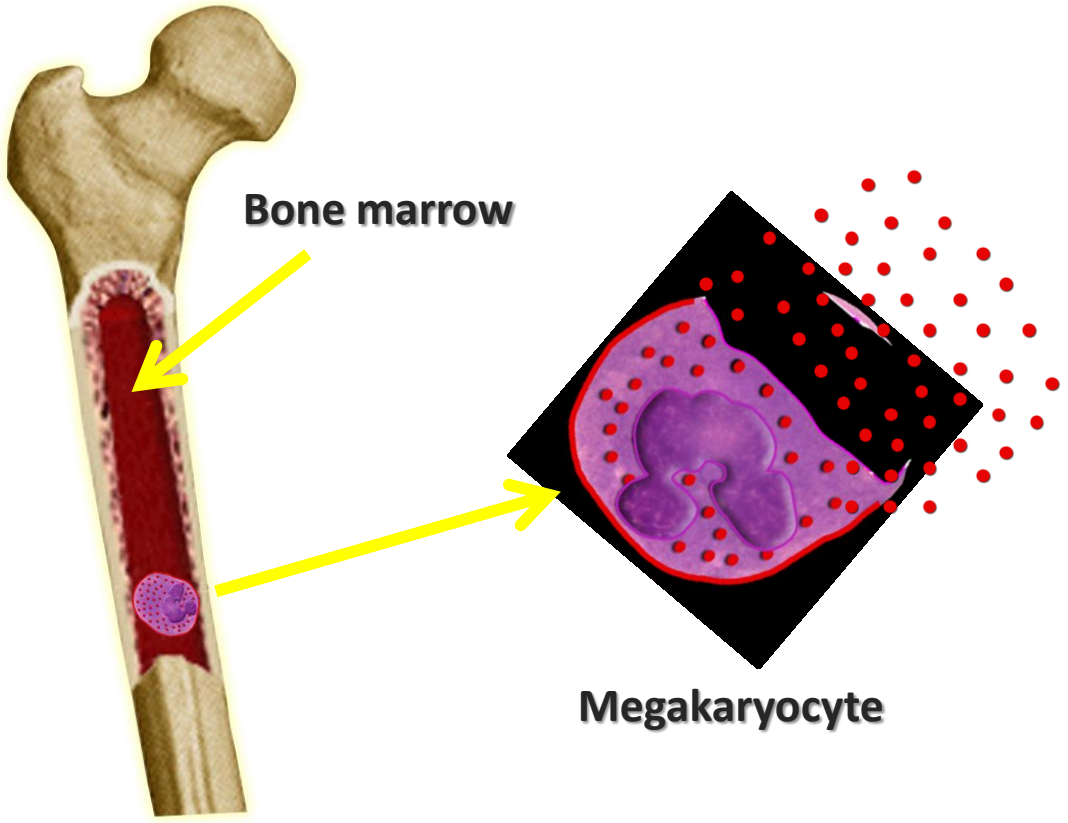
Bone marrow

Platelets Formation (Thrombopoiesis)

Regulation of thrombopoiesis by :

Thrombombopoietin

Platelet covered by glycoprotein that's why they did not stick To each other


Bone marrow
Megakaryocyte
Mature platelets

Platelet ultra-structure (electron microscope – EM)

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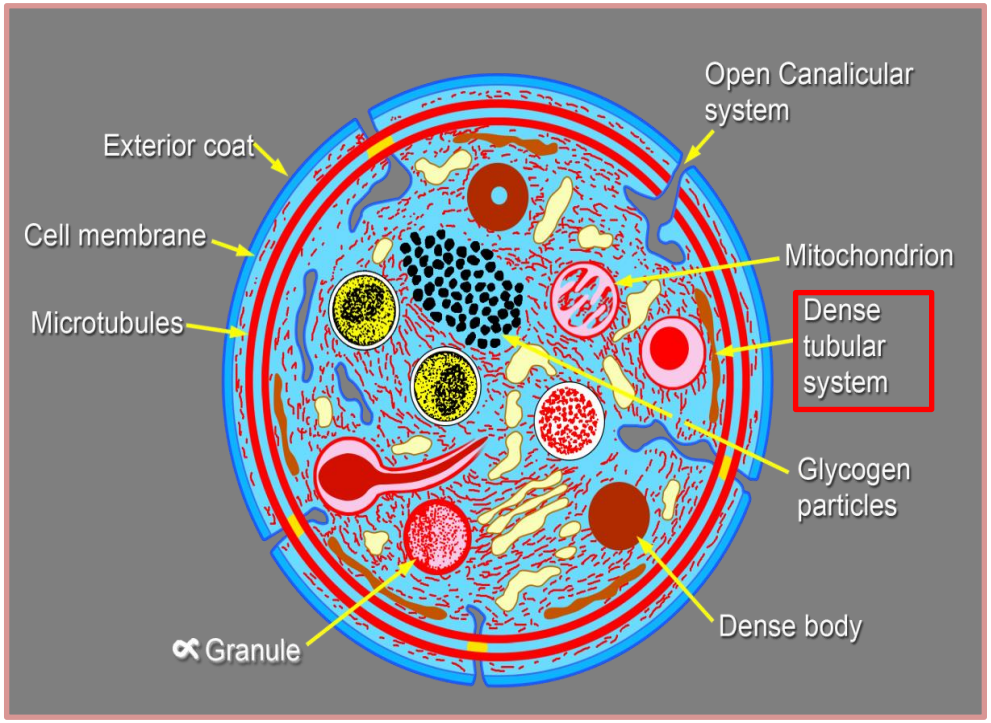
- Anuclear (no nucleus) and discoid cell (inactive) >> spherical when activated.

The dense tubular system responsible for changing the shape of the platelets when they become active.

- Size: 1.5–3.0 µm
- Life span: 7–10 days

Their normal concentration in the blood is between 150,000 and 300,000 /µl

- Sequestered in the spleen; hypersplenism may lead to low platelet counts which lead to bleeding because of the excess destruction by spleen.



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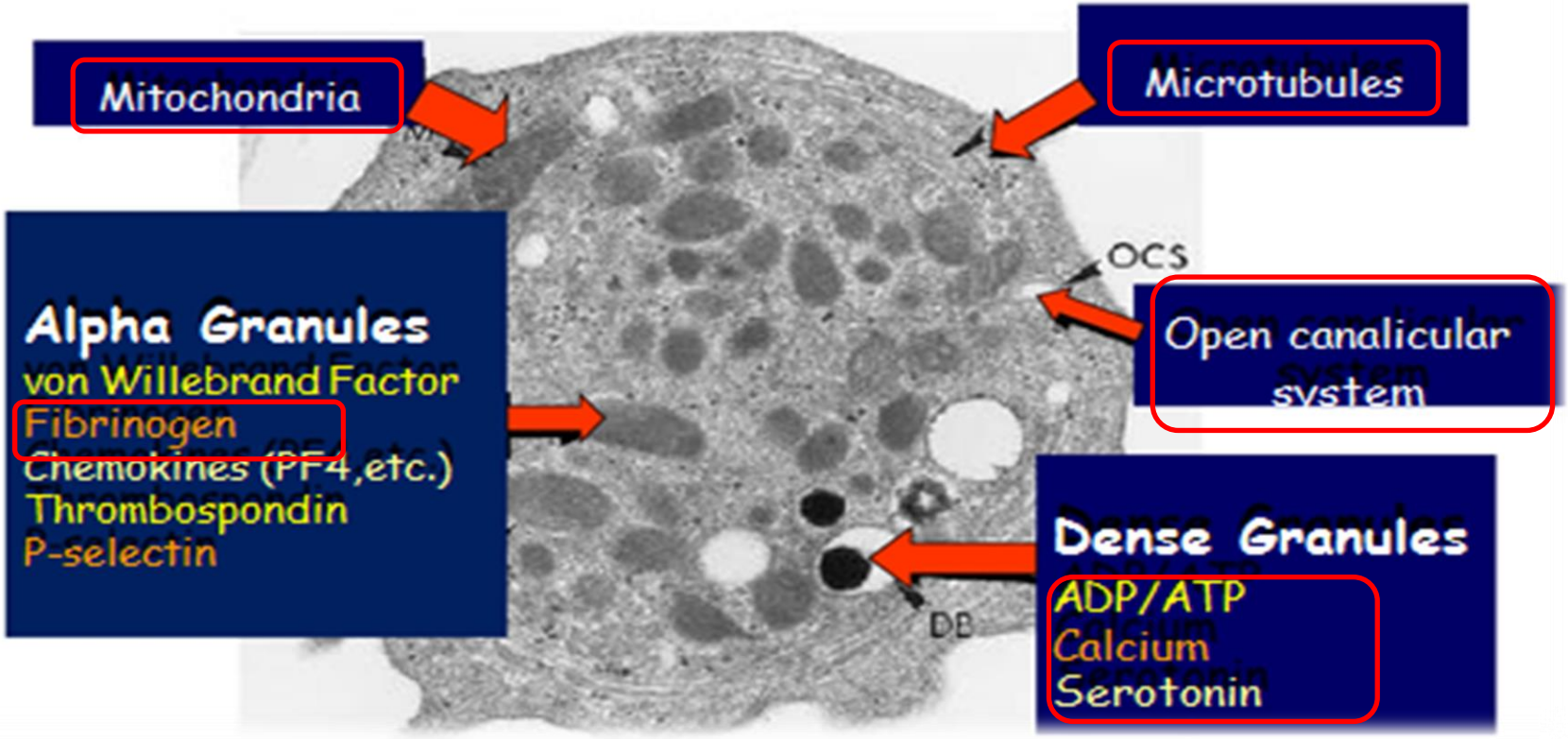
Platelet Ultrastructure



Platelet Receptors :

Important

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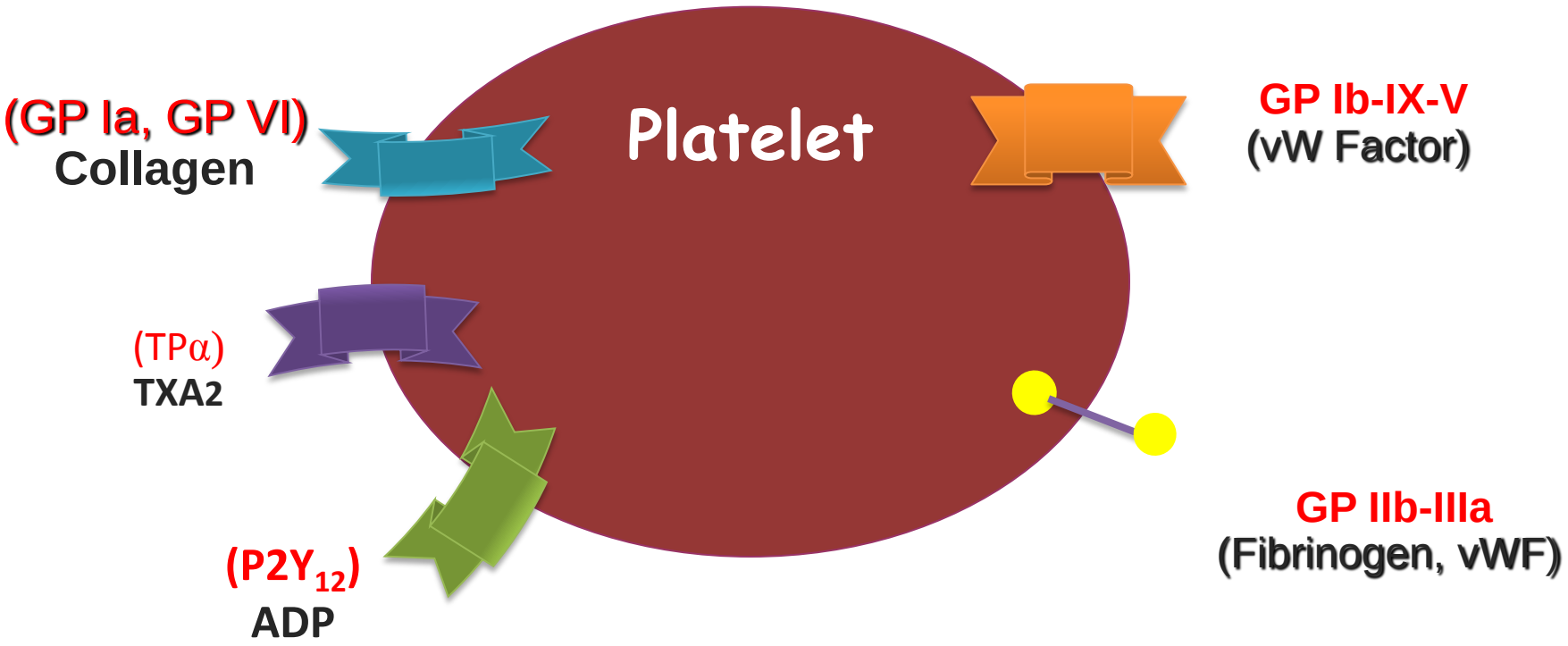

General functions of platelets :

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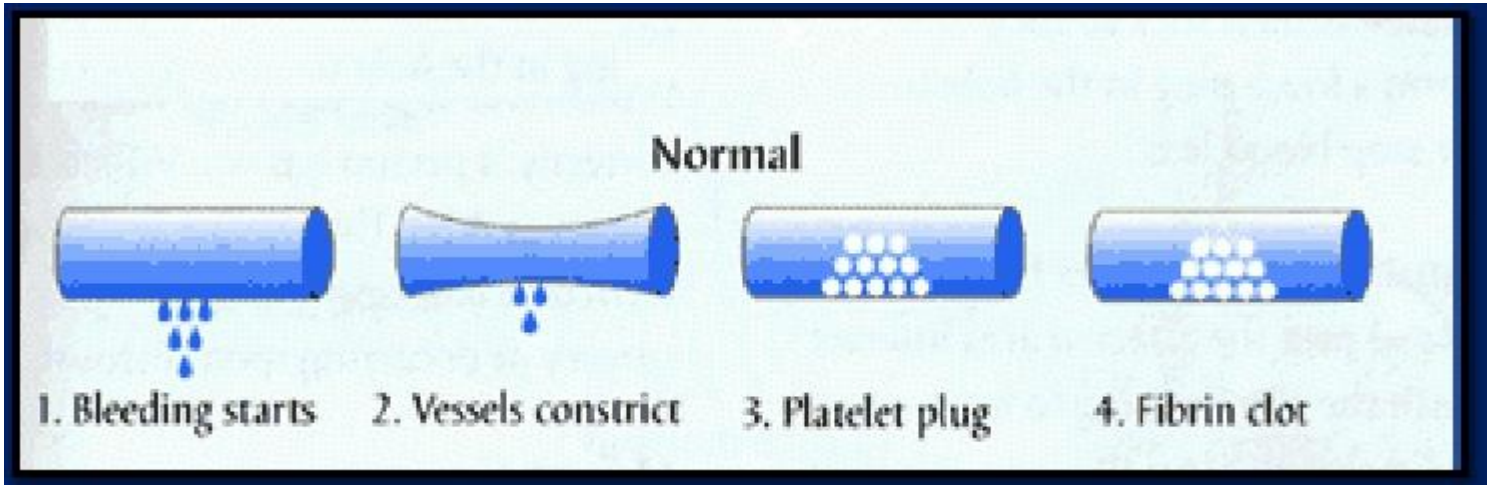
HEMOSTASIS

1. VASCULAR PHASE
2. PLATELET PHASE
3. COAGULATION PHASE
4. FIBRINOLYTIC PHASE



Platelet Activation :

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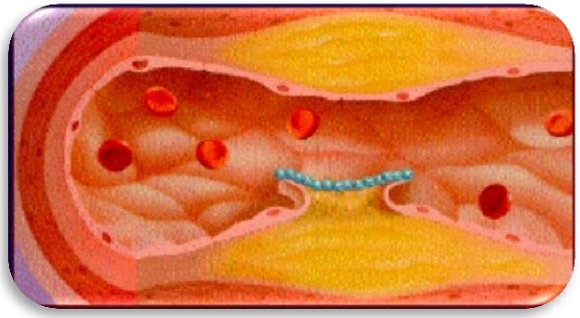
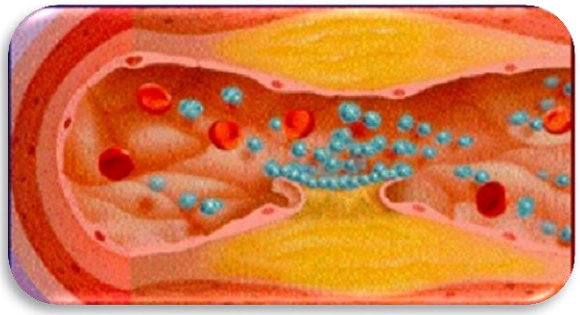
1- Adhesion → 2-Shape change → 3- Aggregation → 4- Release → 5- Clot Retraction

Adhesion



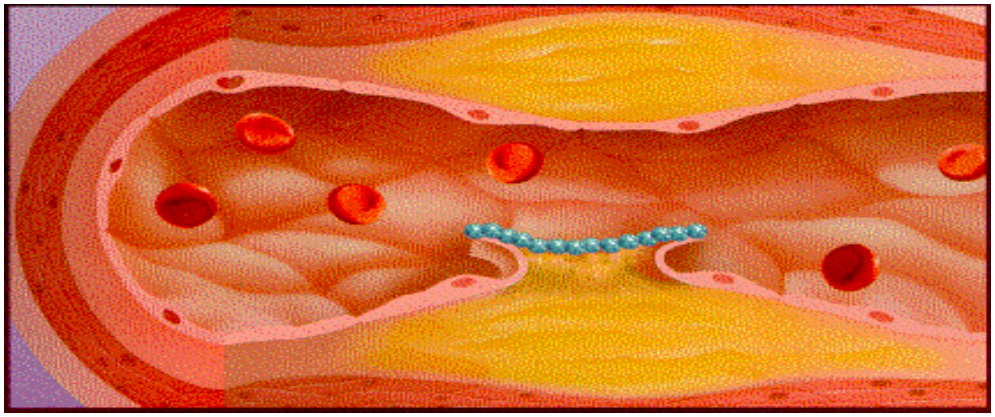
Activation

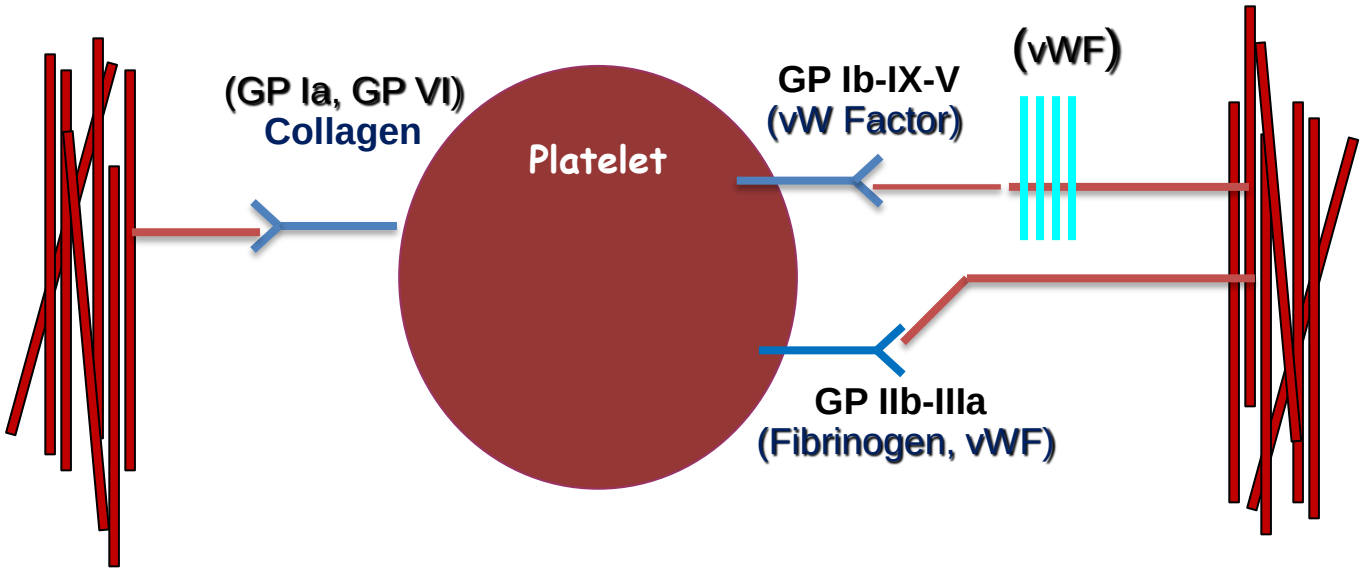


Aggregation

Secretion

1. Adhesion:




(GP Ia, GP VI)
Collagen
Platelet
GP Ib-IX-V
(vW Factor)
(vWF)
GP IIb-IIIa
(Fibrinogen, vWF)

Platelet Aggregation :

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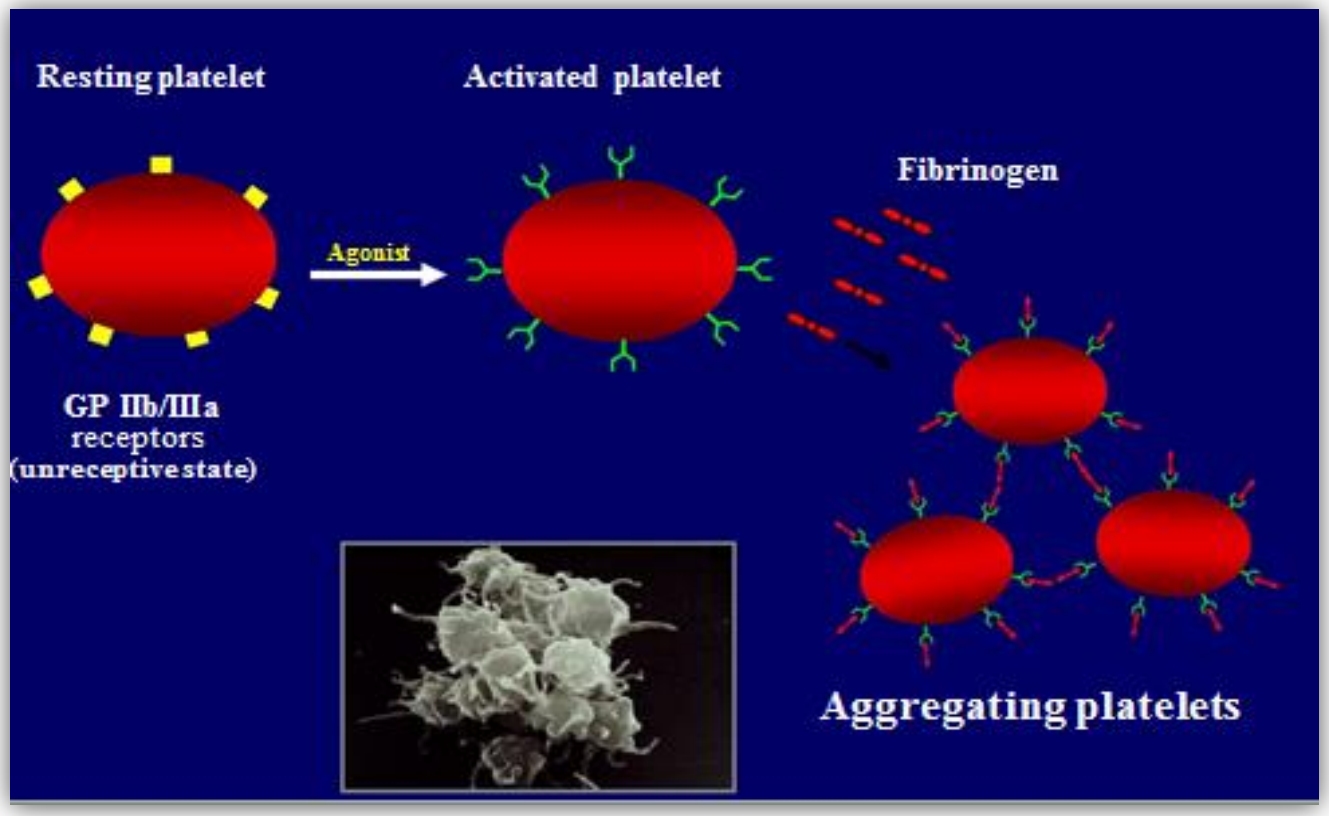
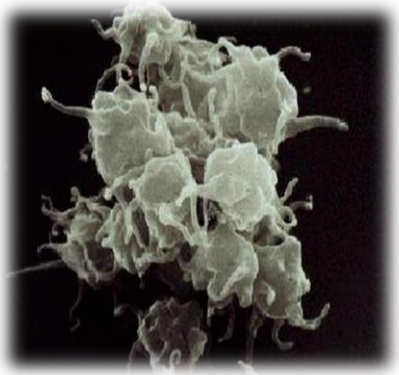
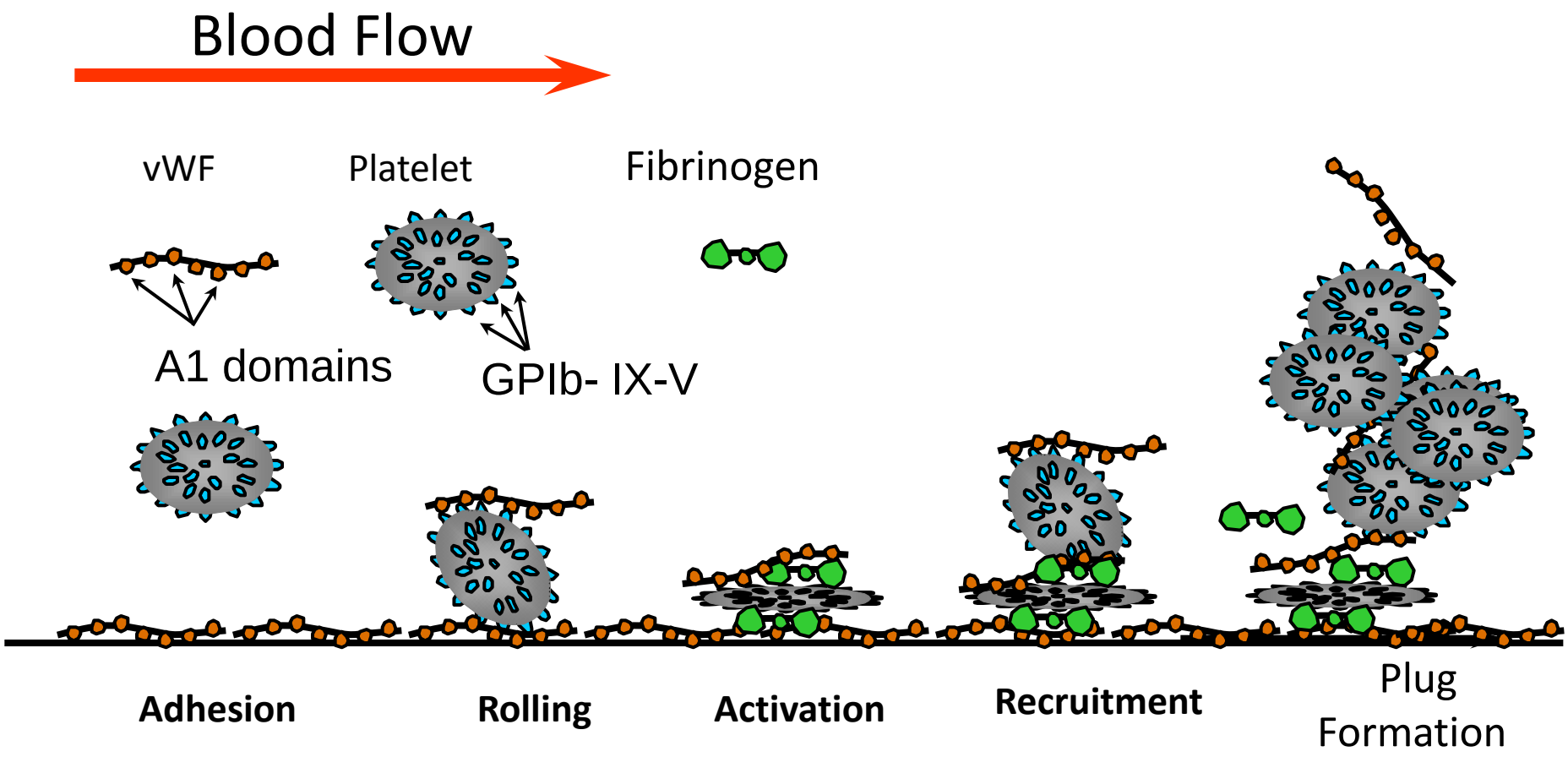
Aggregation:

Fibrinogen is needed to join platelets to each other via platelet fibrinogen receptors.



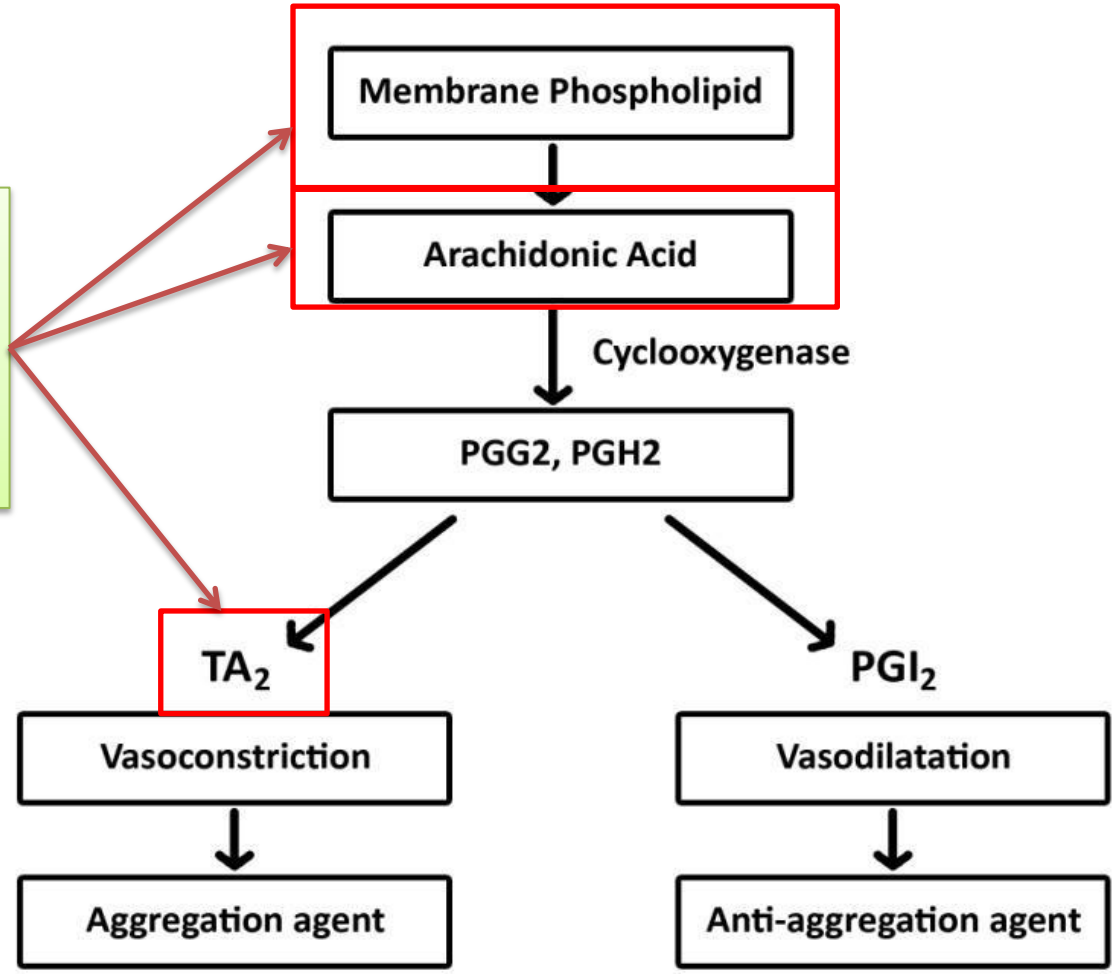


The active platelet has pseudopods.


Blood Flow
vWF
Platelet
Fibrinogen
A1 domains
GPIb- IX-V
Adhesion
Rolling
Activation
Recruitment
Plug Formation

What we have to know from this slide that:

- Thromboxane A2 is coming from AA (Arachidonic Acid)



secrete :

1. 5HT >> vasoconstriction
2. Platelet phospholipid (PF3) >> clot formation.
3. Thromboxane A2 (TXA2) is a prostaglandin formed from arachidonic acid .

Function:

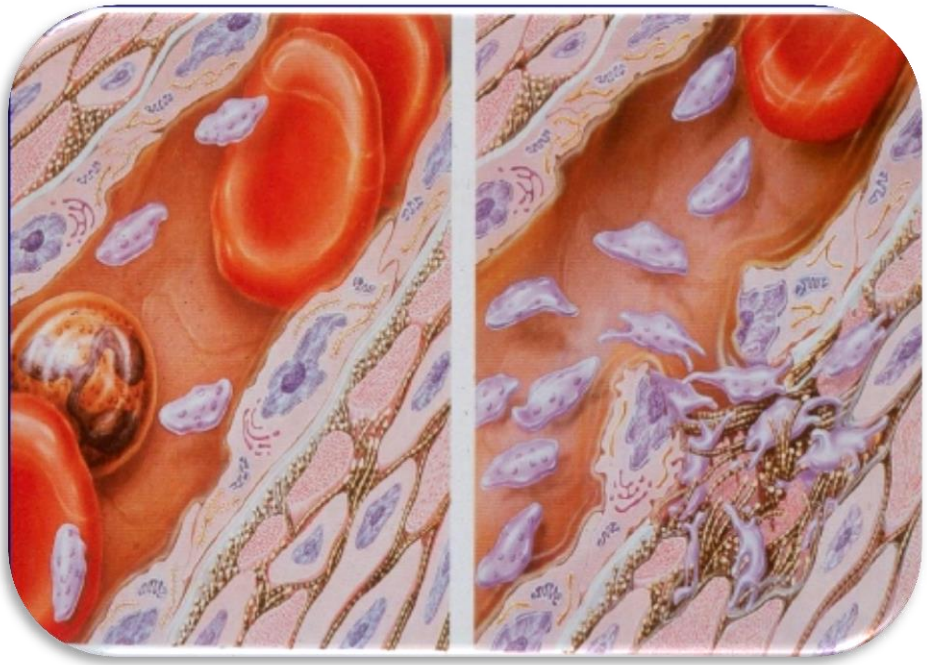
- vasoconstriction .
- Platelet aggregation .

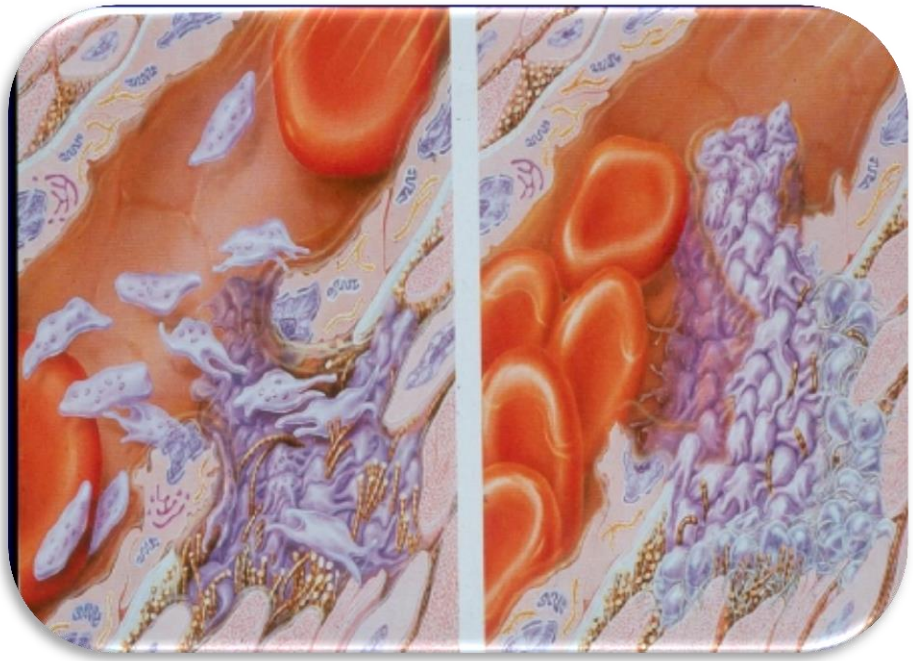
(TXA2 inhibited by aspirin) aspirin decrease the synthesis of TXA2 so this will decrease the aggregation and thrombus formation (protective function especially for heart).

Clot Retraction :

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

Platelet haemostatic plug formation :





- Platelets activated by adhesion.
- Extend projections to make contact with each other.
- Release thromboxane A2, serotonin & ADP activating other platelets.
- **Serotonin & thromboxane A2 are vasoconstrictors** decreasing blood flow.
- through the injured vessel. **ADP causes stickiness** and enhances Aggregation.

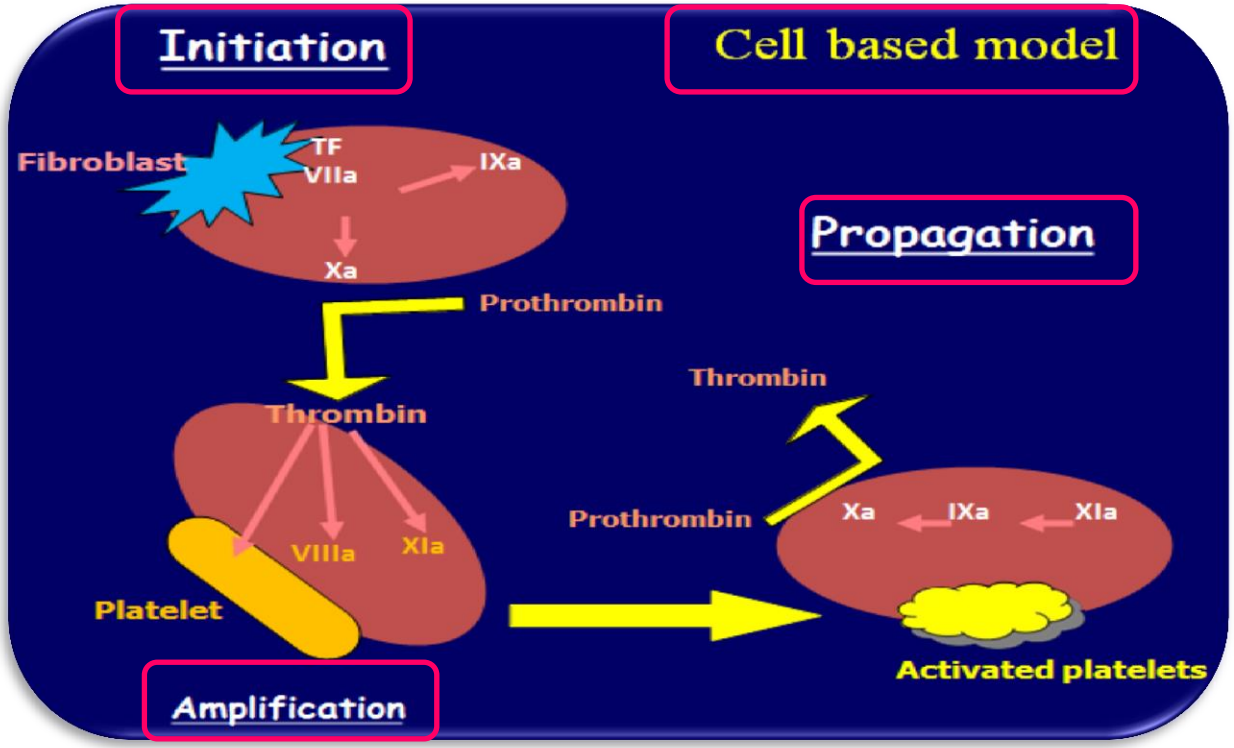
General functions of the platelets:

- Platelet plug formation .
- Platelets and blood coagulation .

Role of platelet in blood coagulation (The cell-based model of blood coagulation) :

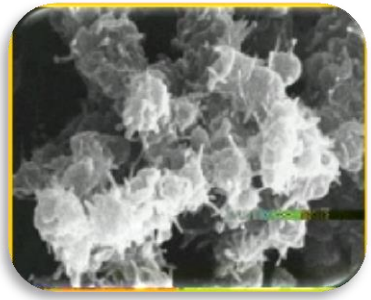
The cell based model has 3 events which happen on the surface of fibroblast and platelet :

1. Initiation.
2. Amplification .
3. Propagation .

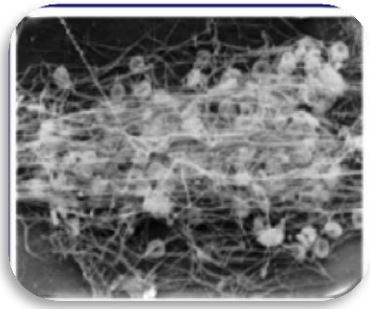


Maintenance of vascular integrity :

Adequate number and function of platelet is essential to participate optimally in Haemostasis .



Initial arrest of bleeding by platelet plug formation .



Stabilization of hemostatic plug by contributing to fibrin formation

Bleeding disorders :

Abnormal number or function of platelet

Bleeding can result from:

– Platelet defects:

- **Deficiency in number (thrombocytopenia)**
- **Defeciency in function (acquired or congenital)**

Platelet function tests :

Laboratory Testing of Platelet Functions :

- ✓ Platelet count & shape.
- ✓ Bleeding time . Normally 30 sec
- ✓ Platelet Aggregation .
- ✓ Platelet Function Analyzer .
- ✓ Flow-cytometry.
- ✓ Electron-microscopy.
- ✓ Granule release products.

Platelet Aggregation (in PRP) platelet rich plasma:

Provides information on time course of plat activation .

Agonists: we add one of these agonists on the blood sample which will stimulate the platelet aggregation .

- ADP
- Adrenaline
- Collagen
- Arachidonic acid
- Ristocetin
- Thrombin

Reference ranges need to be determined for each agonist (+ / - Dose responses)

Congenital Platelet Disorders :

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Disorders of Adhesion:

. Bernard-Soulier Syndrome.

- Receptor: GP Ib-IX-V
- vW Factor

Disorder of Aggregation:

. Glanzmann thrombosthenia

- Receptor: GP Iib-IIIa
- Fibrinogen, vWF

Disorders of Granules:

. Grey Platelet Syndrome .

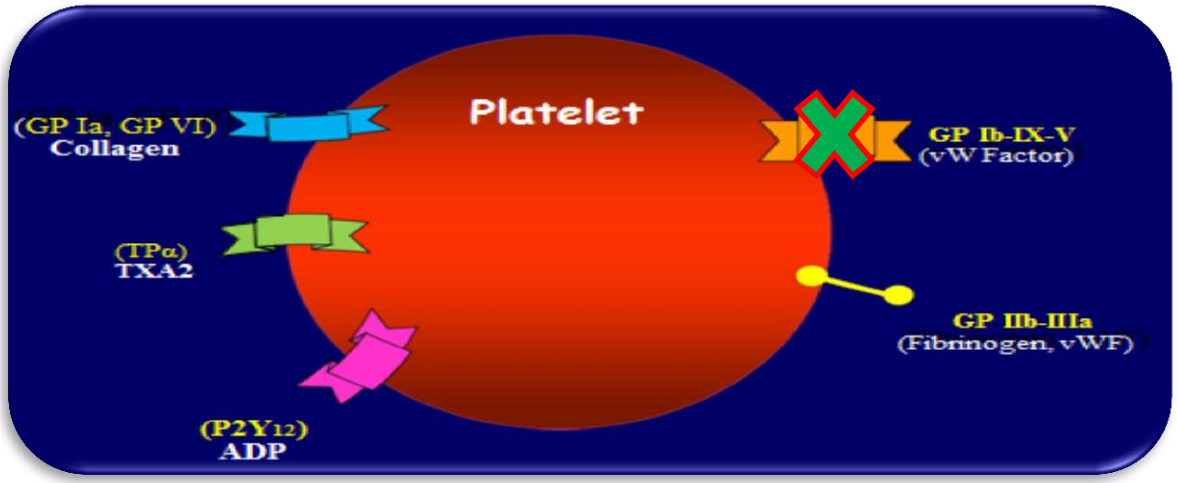
. Storage Pool deficiency .

. Hermansky-Pudlak syndrome .

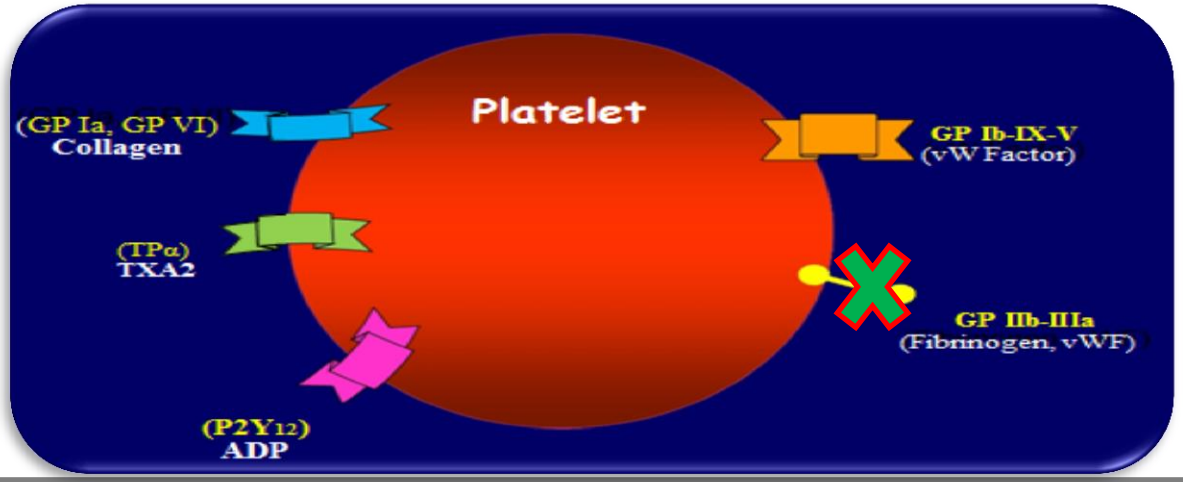
.Chediak-Higashi syndrome .

The defect in that receptor .

Bernard-Soulier Syndrome (BSS) :



Glanzmann thrombosthenia :



Platelet Activation

- 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 phospholipids to 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

SUMMARY

- Platelets are cell fragments derived from megakaryocyte in the bone marrow
- Thrombopoietin is synthesized in the liver

- Platelets play a pivotal role in hemostasis by arresting bleeding from injured blood Vessels.

- The first stage of hemostasis is adhesion

- Bleeding can result from: Platelet defects *acquired* or *congenital:*

Disorders of Adhesion:

. Bernard-Soulier Syndrome

Disorder of Aggregation:

. Glanzmann thrombosthenia

QUESTIONS

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1. The first stage in platelet activation is:

A. Adhesion
B. aggregation
C. Secretion
D. clot retraction

2- which one of the following is responsible for joining the platelets to each other ?

A. VWF
B. fibrinogen
C. Collagen
D. ADP

3- Which of the following receptors is responsible for aggregation ?

A. GP Ib-IX-V
B. GP IIb-IIIa
C. P2Y12
D. TP alpha

4- one of the following is a component of Dense granules :

A. VWF
B. Ca
C. Fibrinogen
D. p- selectin

A
B
B
B

THE END

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If there are any Problems or Suggestions,
Feel free to contact us:

Physiology Team Leaders

Mohammed Jameel & Shaimaa Al-Refaie

432Physiology@gmail.com

THANK YOU

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