11
Platelet Structure & Function

MED 433 Teams

GIT

Objectives

- 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

New terms :

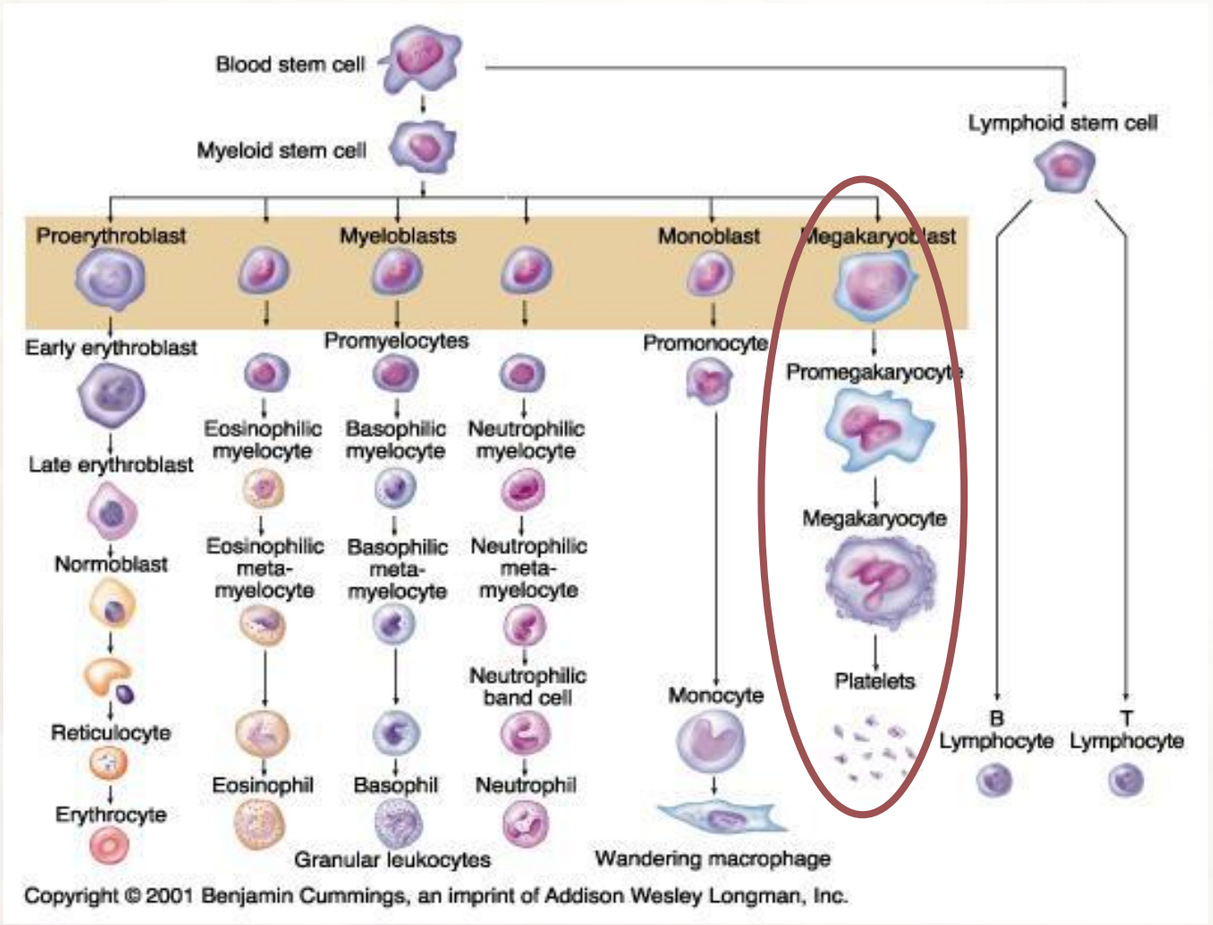
- GP = glyco protein
- vW factor = von Willebrand factor
- TXA2 = Thromboxane A2

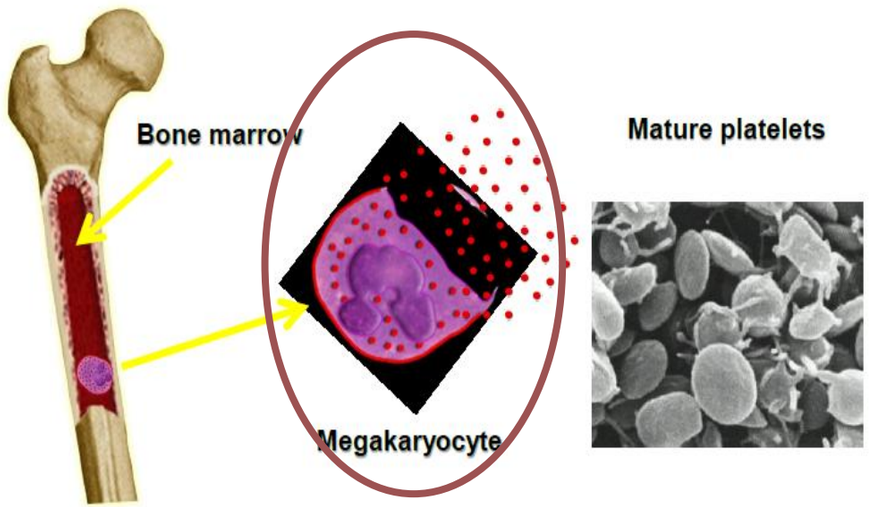
Remember to differentiate between:

- Haemostasis = stoppage of bleeding
- Homeostasis = balance

Site of formation :

in the bone marrow by the stem cell → megakaryoblast → megakaryocyte (the hugest cell) → platelets





The megakaryocyte contains the platelet → it will break down and release the platelets into the circulation

The formation of the platelets called Thrombopoiesis and it is regulated by Thrombopoietin (from the liver)

Platelet ultr-structure:

-It is anuclear (no nucleus) and discoid cell in when it isn't active → spherical shape when it is activated

-OCS : * increases the surface area during the bleeding .

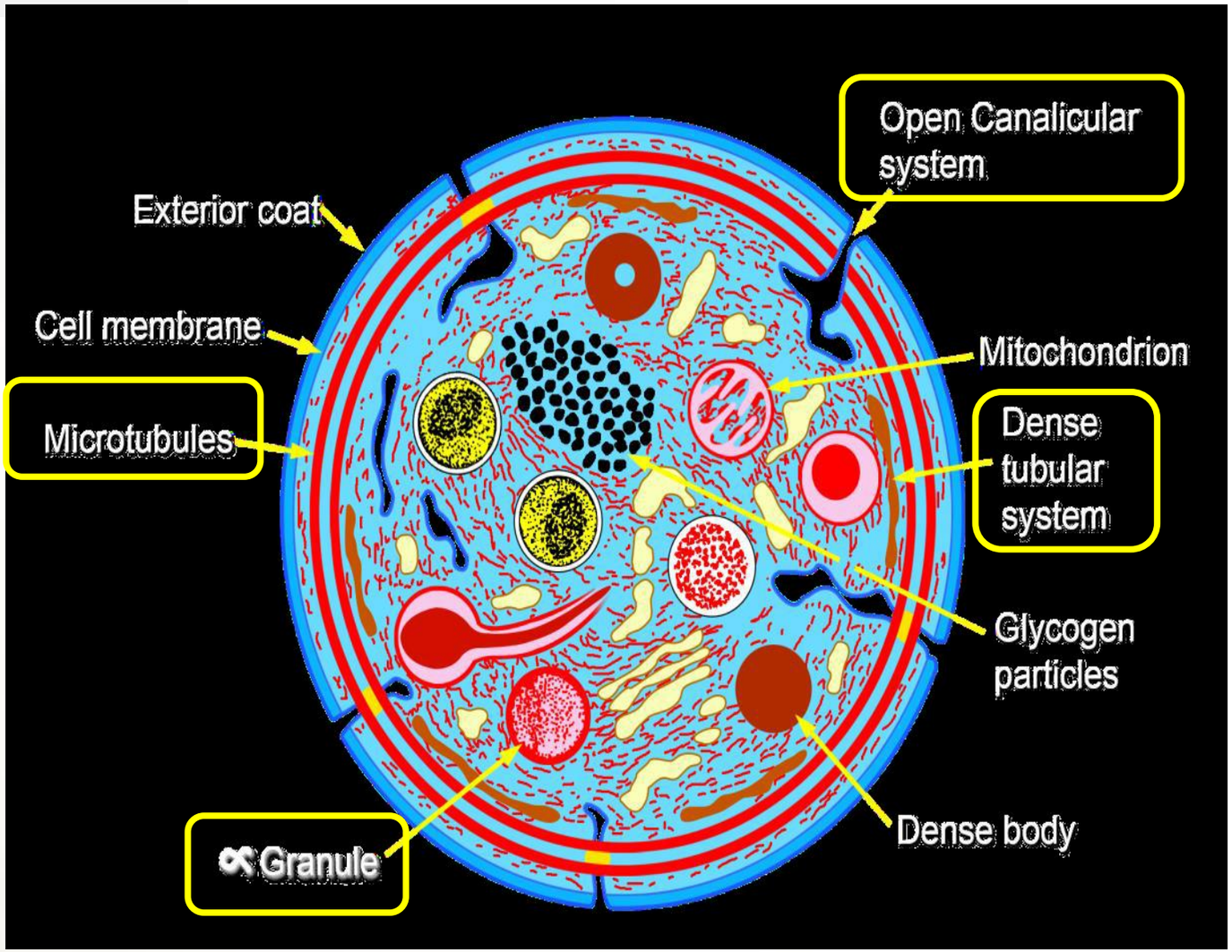
* passage of the platelet secretion .

-Alpha granule = like bags in side the cell which contains :

- ❖von Willebrand Factor
- ❖Fibrinogen

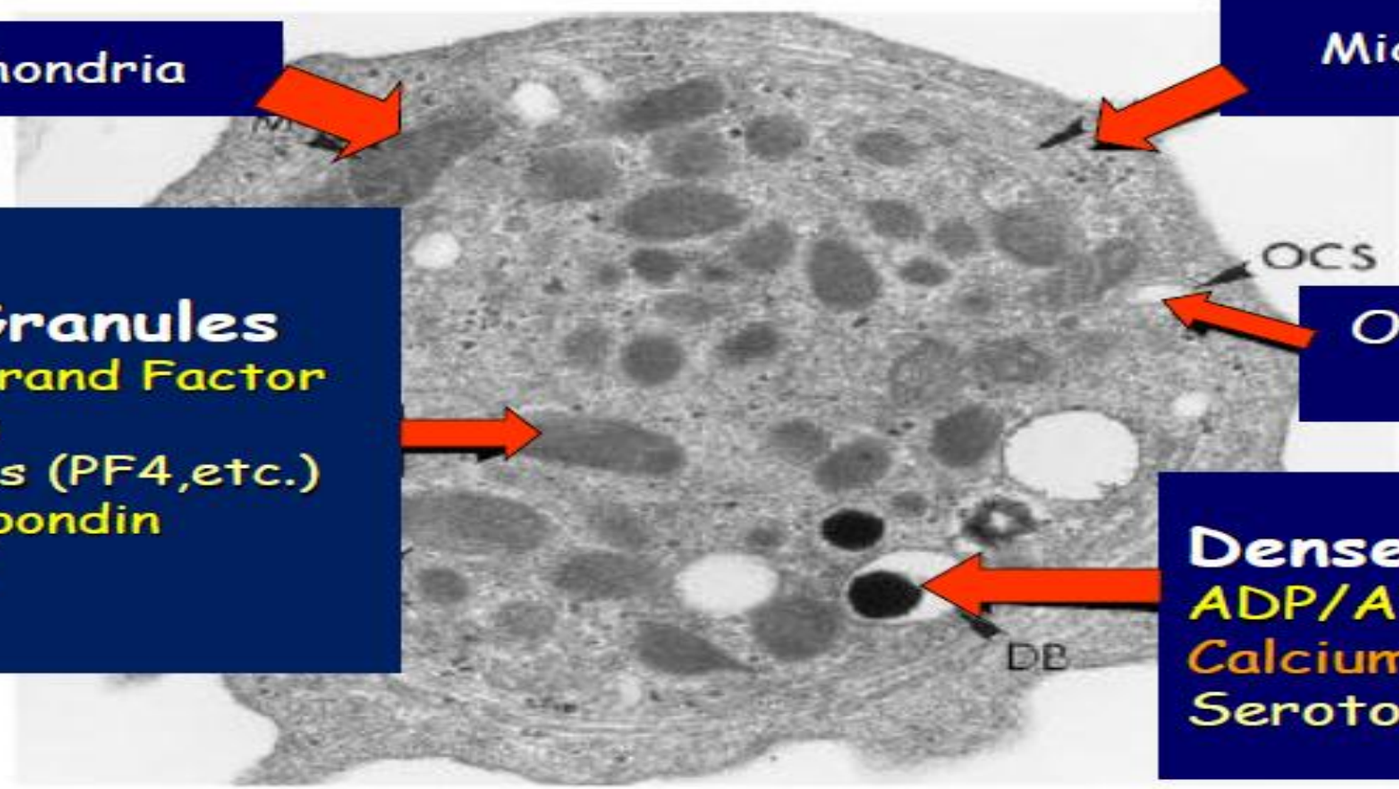
-The Dense tubular system responsible for changing the shape of the platelets when they become active

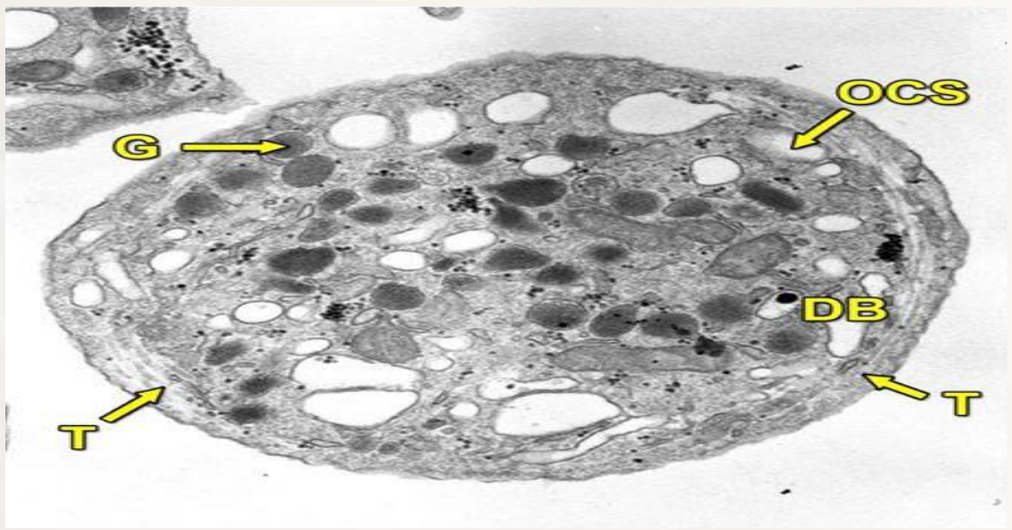
•Sequestered in the spleen;
hypersplenism may lead to low platelet counts لانه تتم ازالة الصفائح الدمويه عن طريق الطحال وهذا الخلل في عمل الطحال يؤدي الى ازالة الصافائح الصالحه والفاسده من الدم مما قد يسبب نزيف لعدم وجود مايكفي من الصائح لوقف النزي

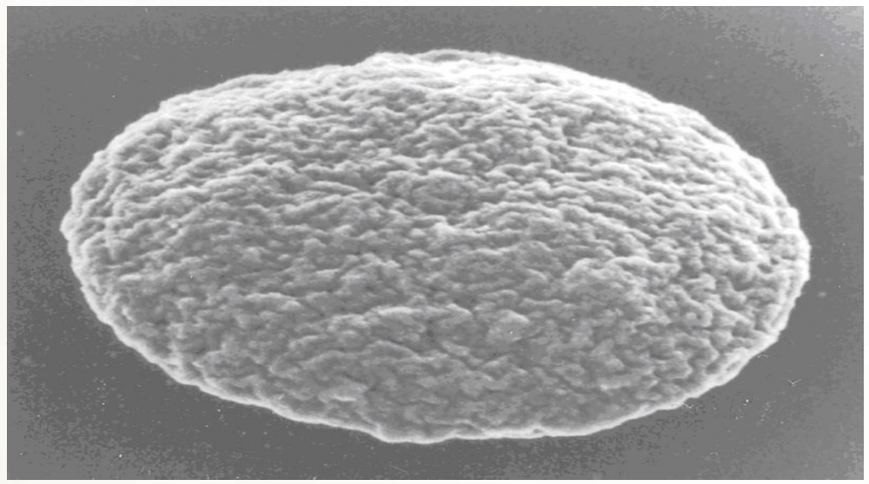


- •Platelet count = 150 x103-300x103/ml
- •Size: 1.5–3.0 µm
- •Life span: 7–10 days

Platelet Ultrastructure

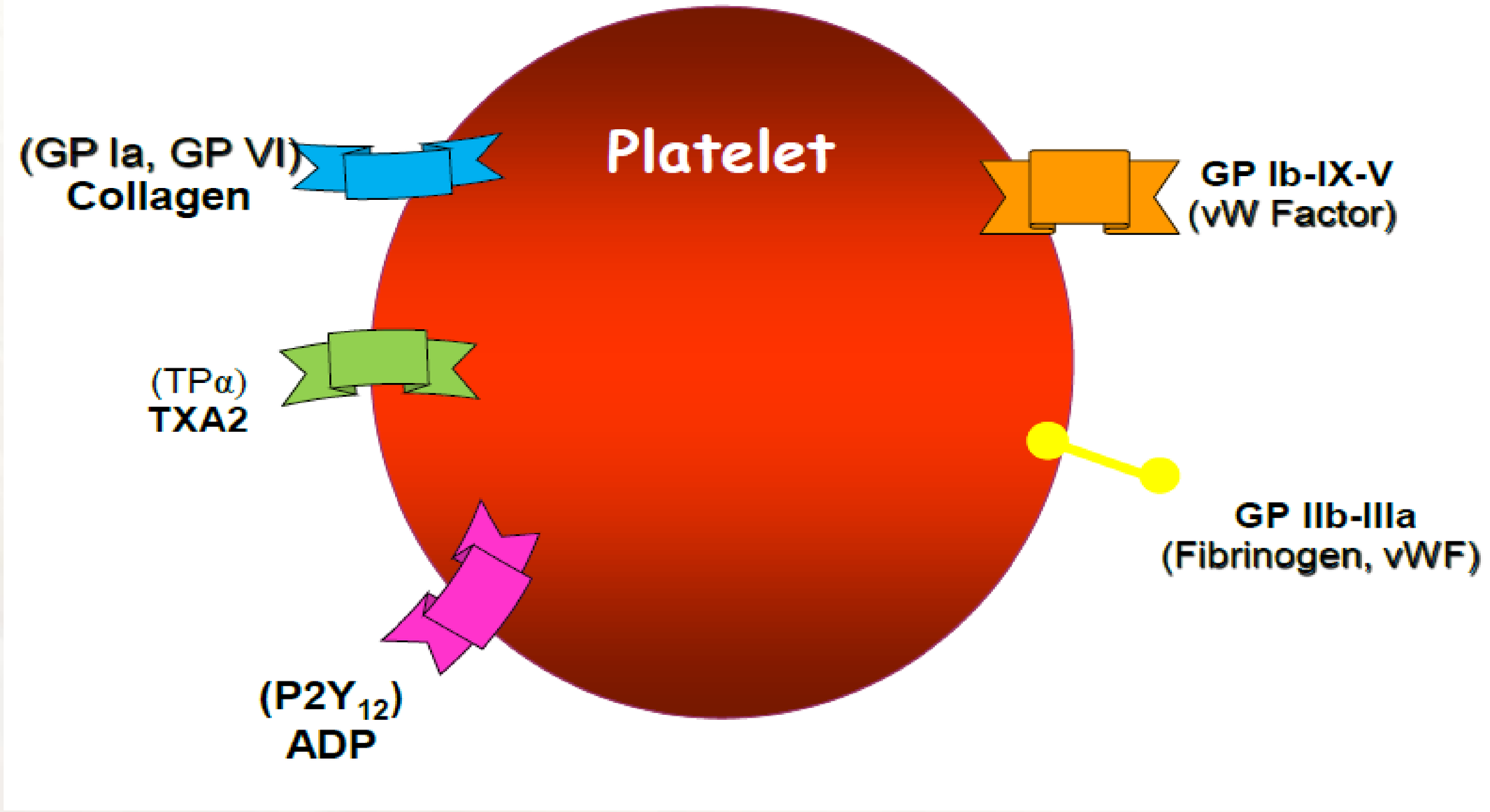






It looks like the brain

Platelet receptors:



General functions of the platelets :

1. Initial arrest of bleeding by platelet plug formation (haemostasis)
2. Platelets and blood coagulation

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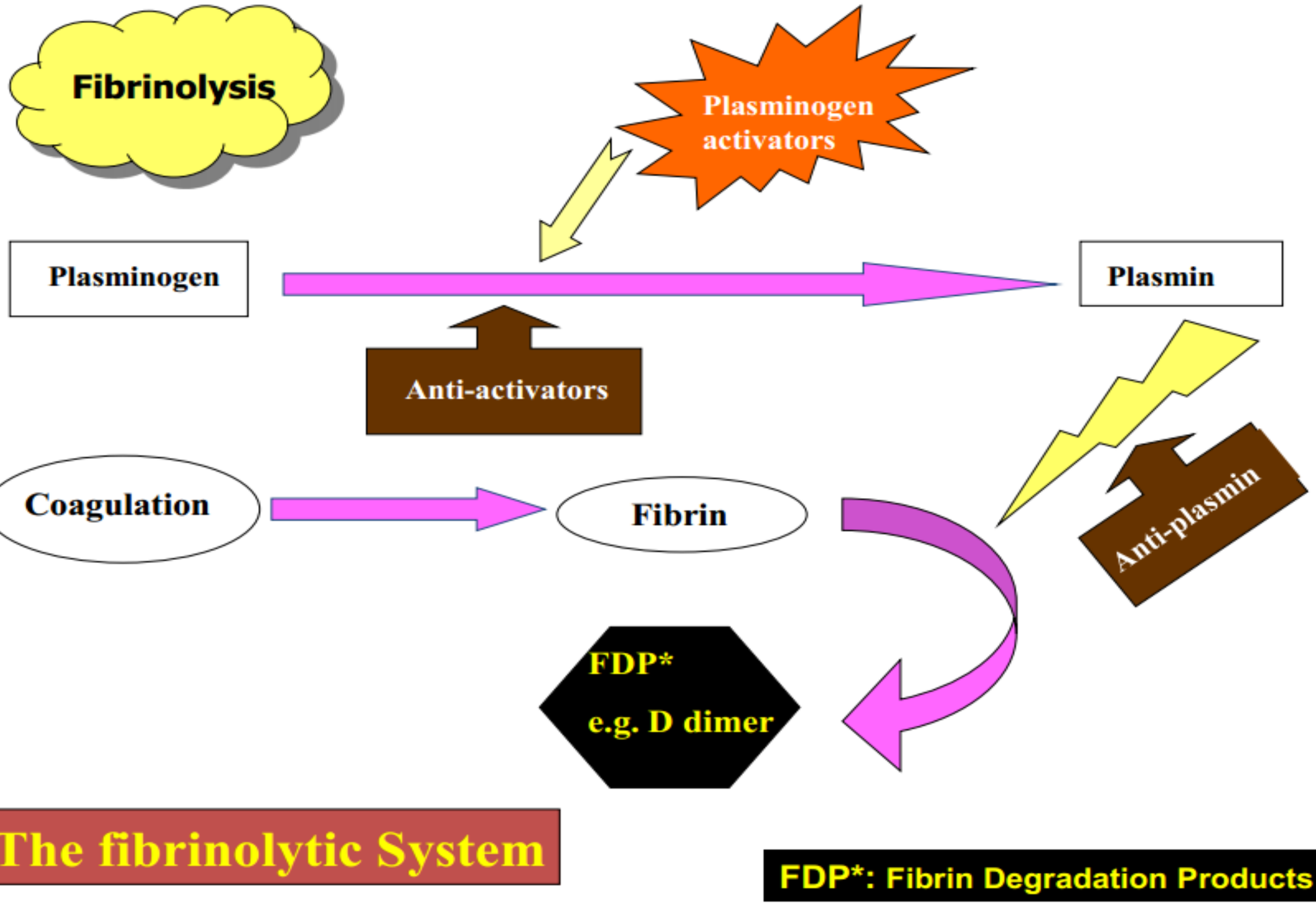
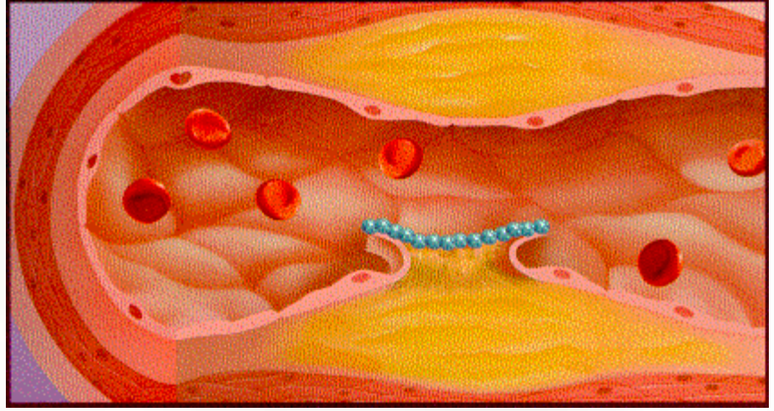
1. Initial arrest of bleeding by platelet plug formation (haemostasis)

Vascular phase	Platelet phase	Coagulation phase	Firbrinolytic phase
Vasoconstriction of the injured vessel and reflex constriction of the adjacent small arteries and arterioles → to decrease blood flow	Platelets activation : ❖ adhesion ❖ shape change ❖ aggregation ❖ release reaction ❖ clot retraction	-A series of biochemical reactions leading to the formation of a blood clot → eads to the activation of thrombin enzyme from inactive form Prothrombin → Thrombin will change fibrinogen (plasma protein) to fibrin (insoluble protein) → formation of secondary haemostatic plug	-Break down of fibrin by naturally occurring enzyme plasmin therefore prevent intravascular blocking . -There is balance between clotting and fibrinolysis . *Excess clotting → blocking of Blood Vessels *Excess fibrinolysis → tendency for Bleeding


Fibrinolysis
Plasminogen activators
Plasminogen
Plasmin
Anti-activators
Coagulation
Fibrin
Anti-plasmin
FDP*
e.g. D dimer
The fibrinolytic System
FDP*: Fibrin Degradation Products

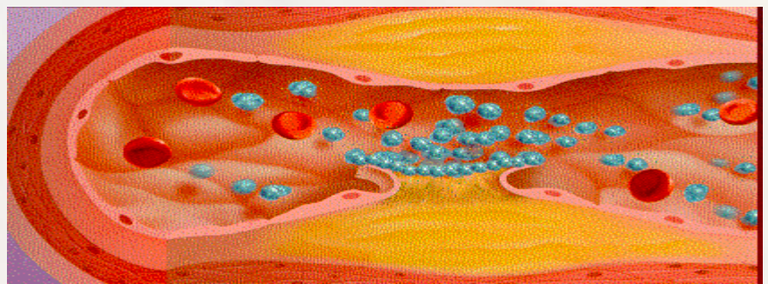
Adhesion :

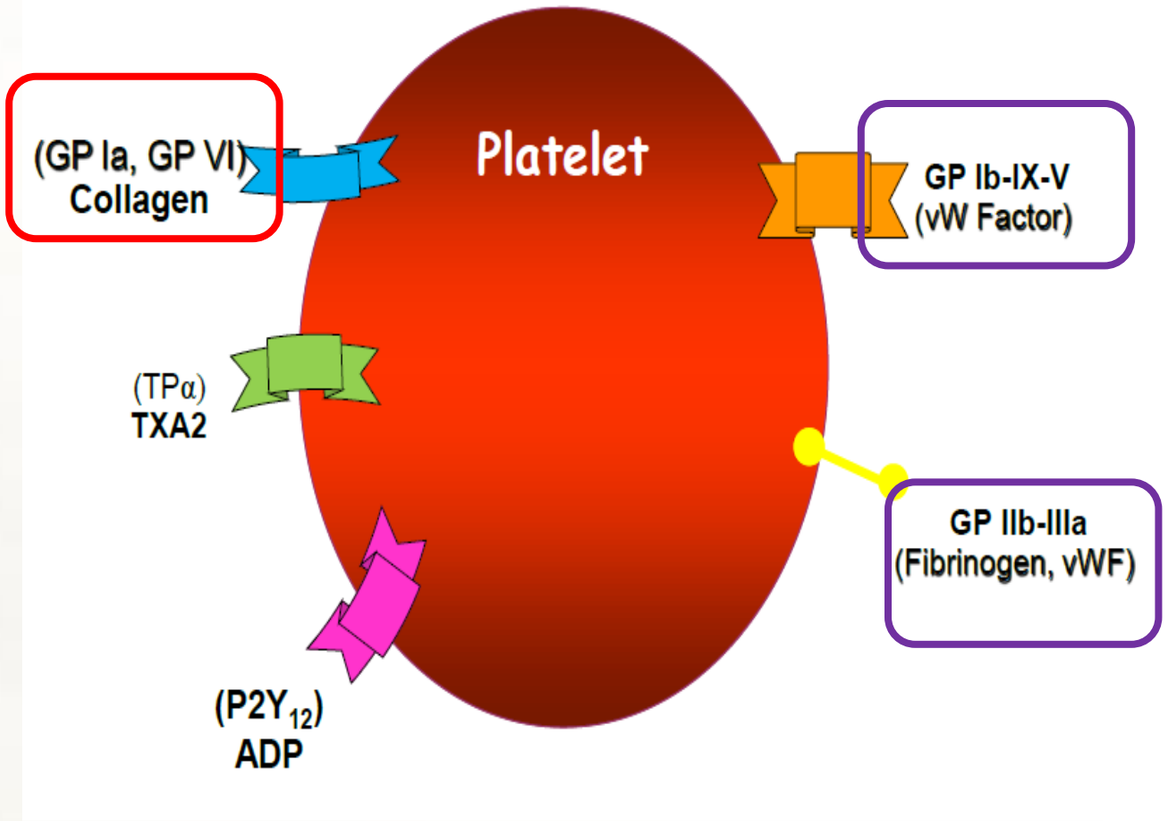


Platelets stick to exposed collagen underlying damaged endothelial cells in vessel wall
By to ways :

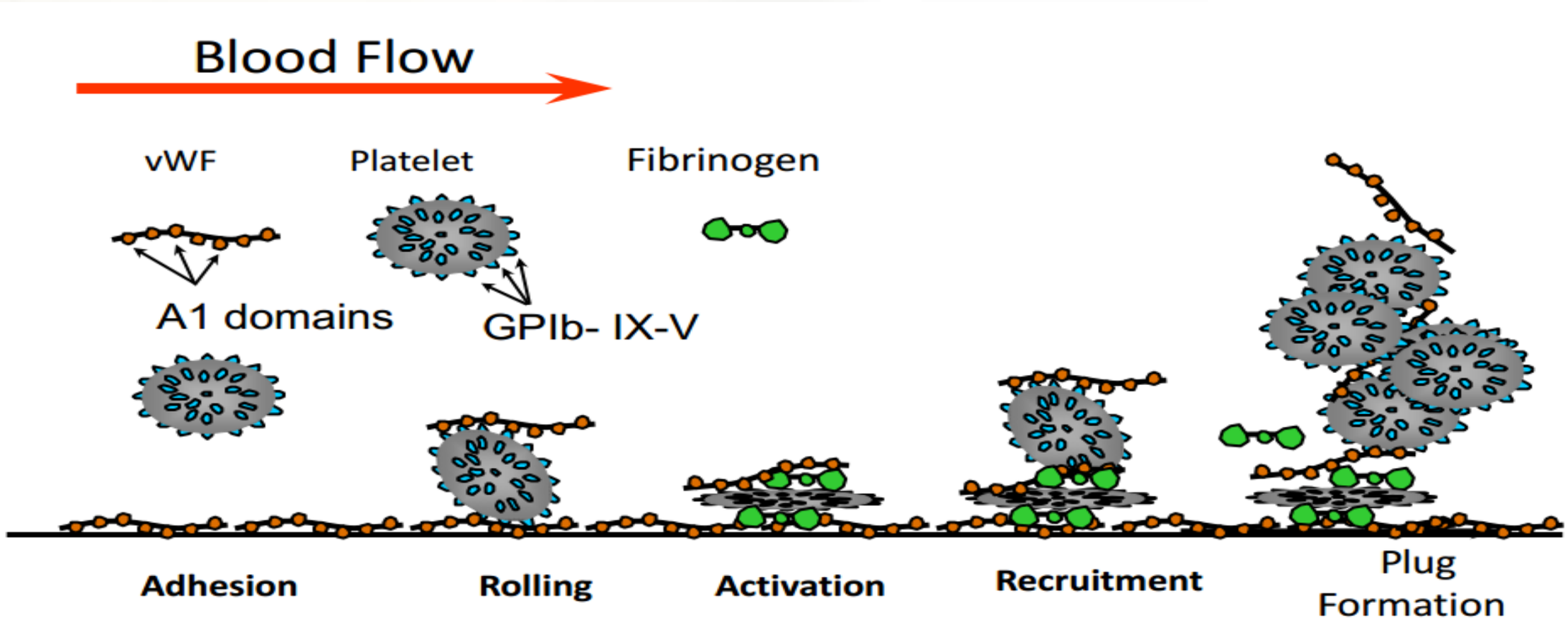
***Direct way through (GP Ia,GP VI) receptor**
*** indirect through vW factor**

After that the platelets will be activated and release its contents and also activate platelets prostaglandin synthesis leading to the formation of TXA2 (will be discussed in further slide)





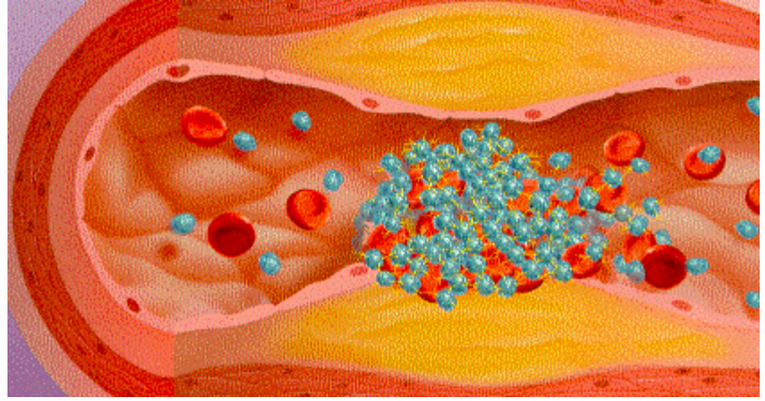
von Willebrand factor (vWF) and Platelet Adhesion :



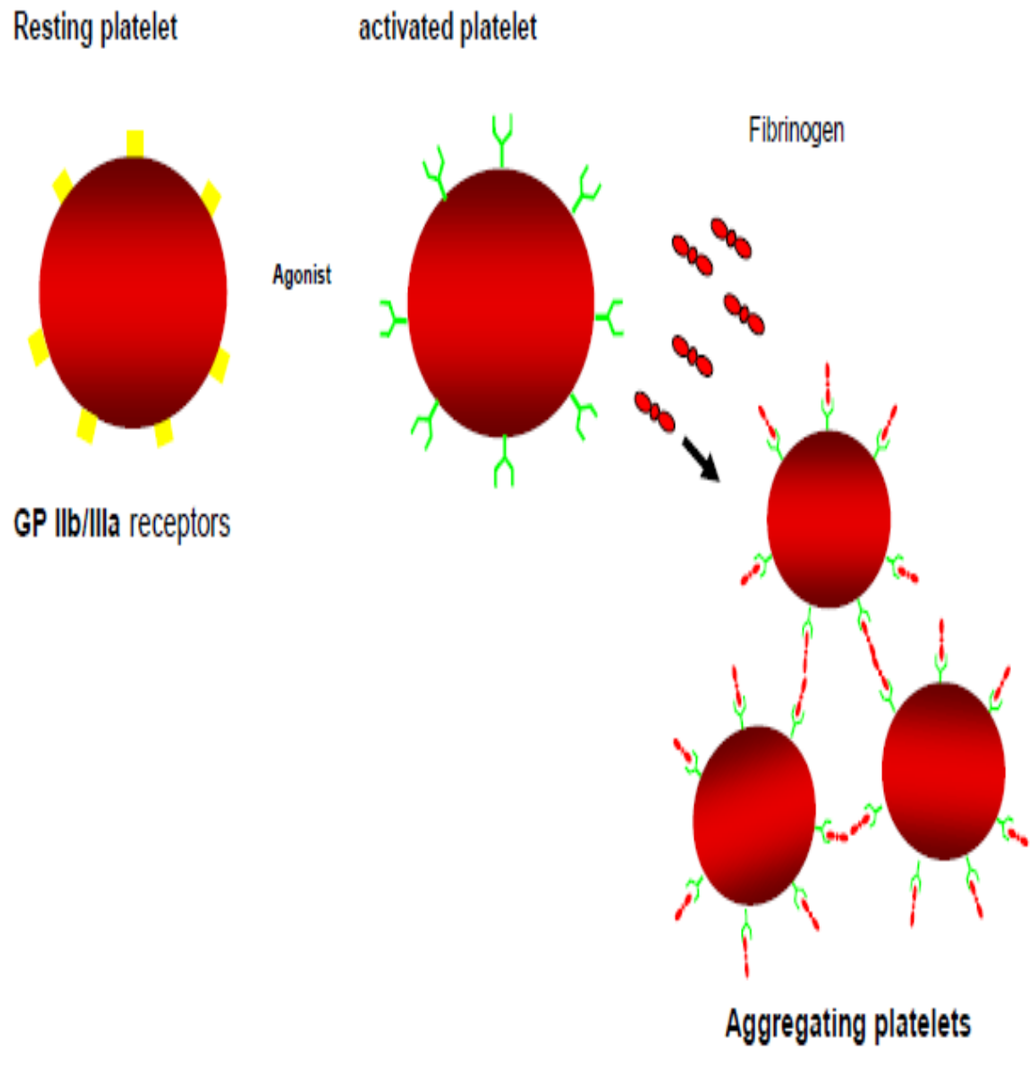
From Med432 team work

Platelets aggregation :

1. Activation of the platelets will lead to secret its contents one this contents is ADP which causes platelets swelling and aggregation (sickness) .
2. Also TXA2 causes platelets aggregation



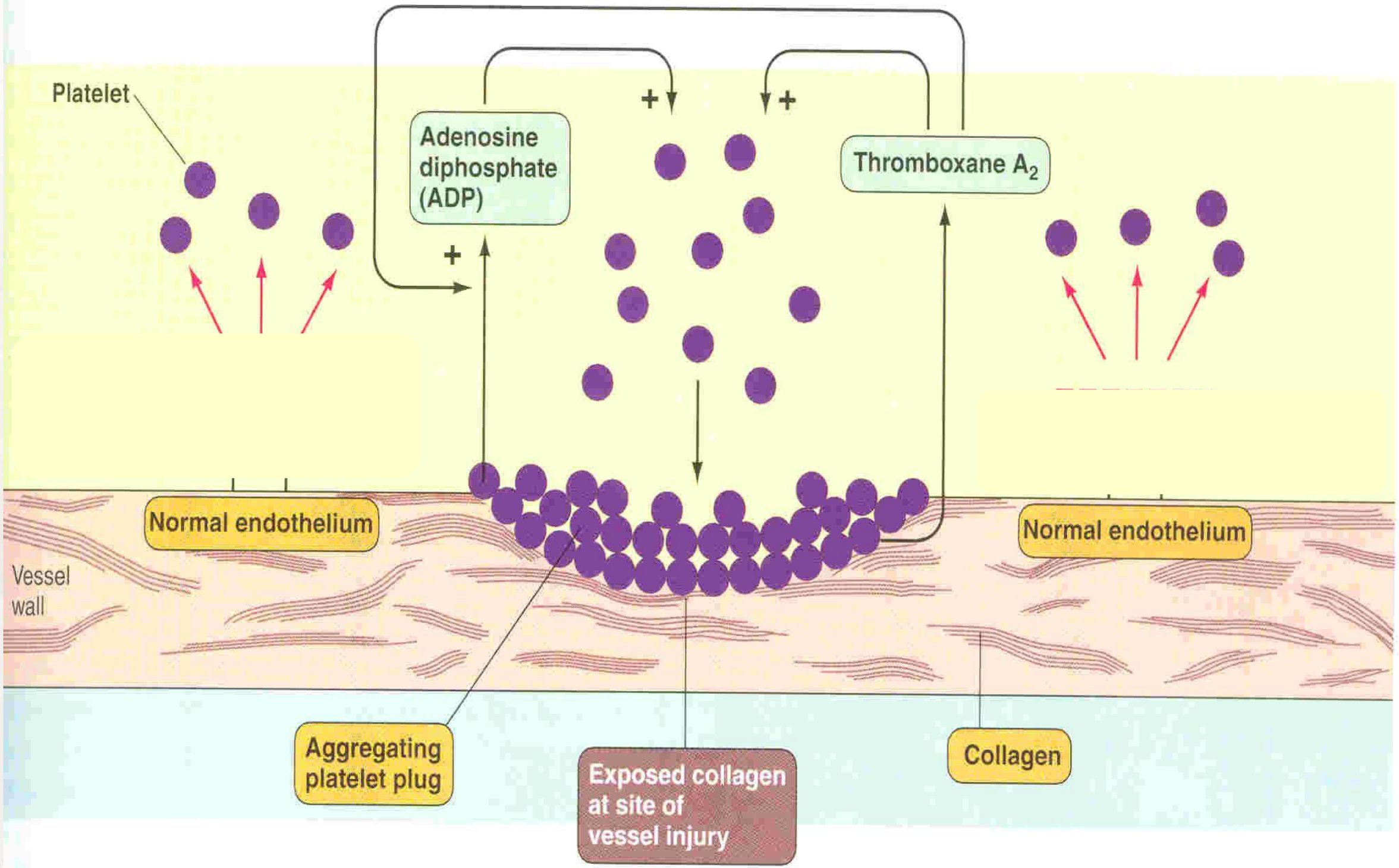
Fibrinogen is needed to join platelets to each other via platelet fibrinogen receptors



Remember this interaction is between the platelets only

http://youtu.be/0pnpoEy0eYE

Platelets aggregation :

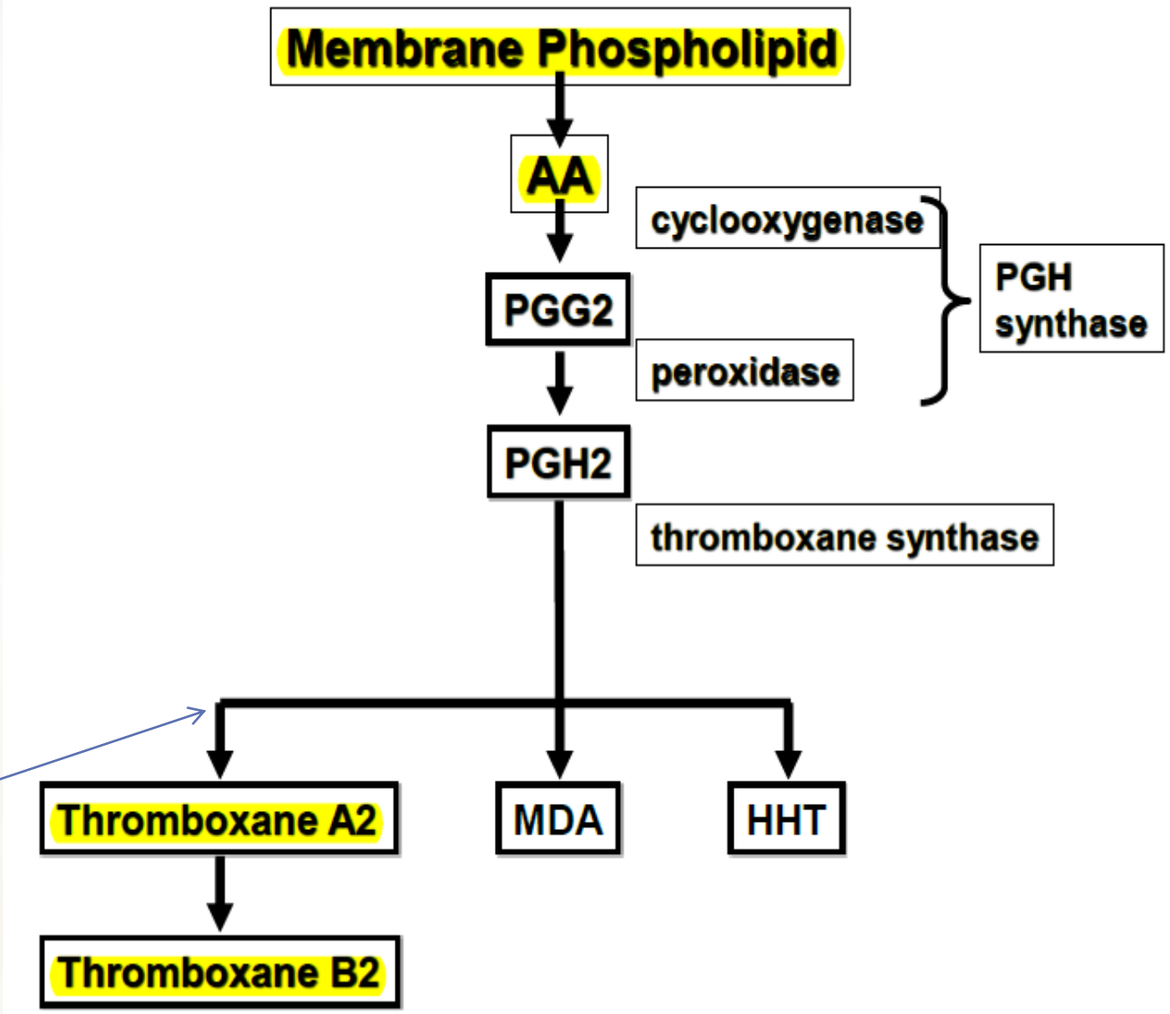


platelets secretions :

Platelets activated by adhesion, Extend projections to make contact with each other , and release :

1. ADP
2. 5HT → vasoconstriction
3. Platelet phospholipid (PF3)→clot formation
4. Thromboxane A2 (TXA2) is a prostaglandin formed from arachidonic acid (AA) Function:

- Vasoconstriction
- Platelet aggregation

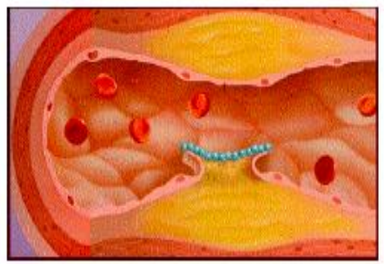


(TXA2 inhibited by aspirin)
Because aspririn aspirin decrease the synthesis of TXA2 so this will decrease the aggregation and thrombus formation use as prophylactic in heart disease

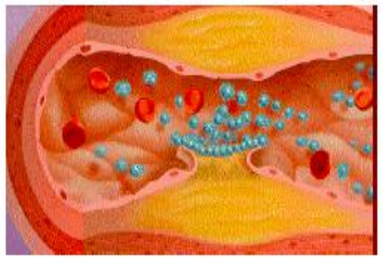
You have to know the highlighted words

Clot retraction :

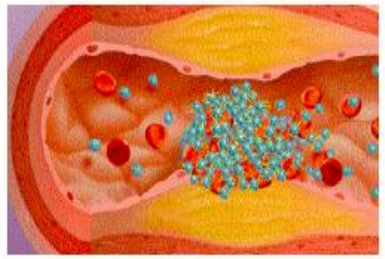
Myosin and actin filaments in platelets are stimulated to contract during aggregation further reinforcing the plug and help release of granule contents



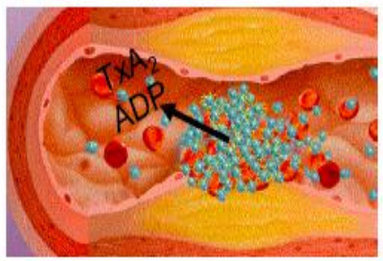
Adhesion



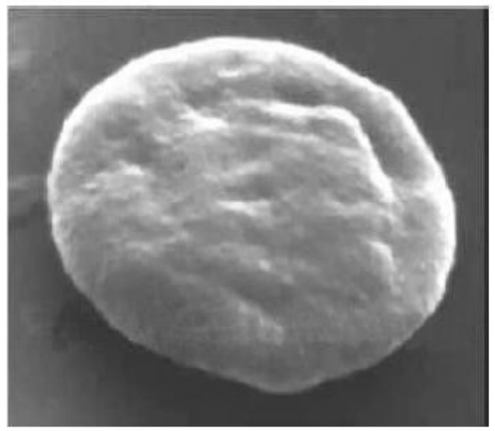
Activation

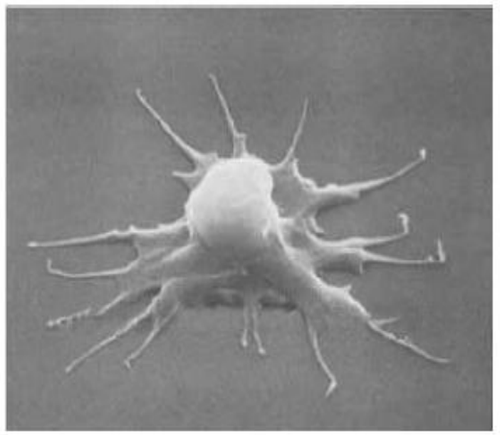


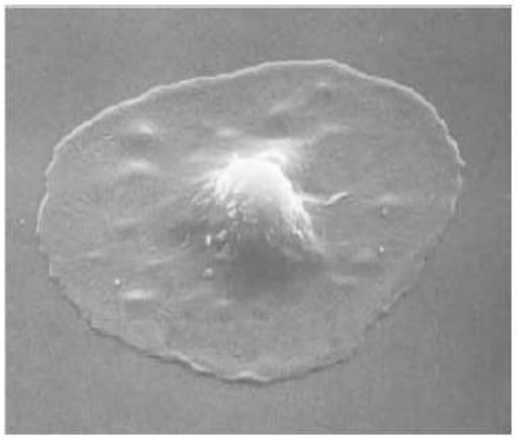
Aggregation



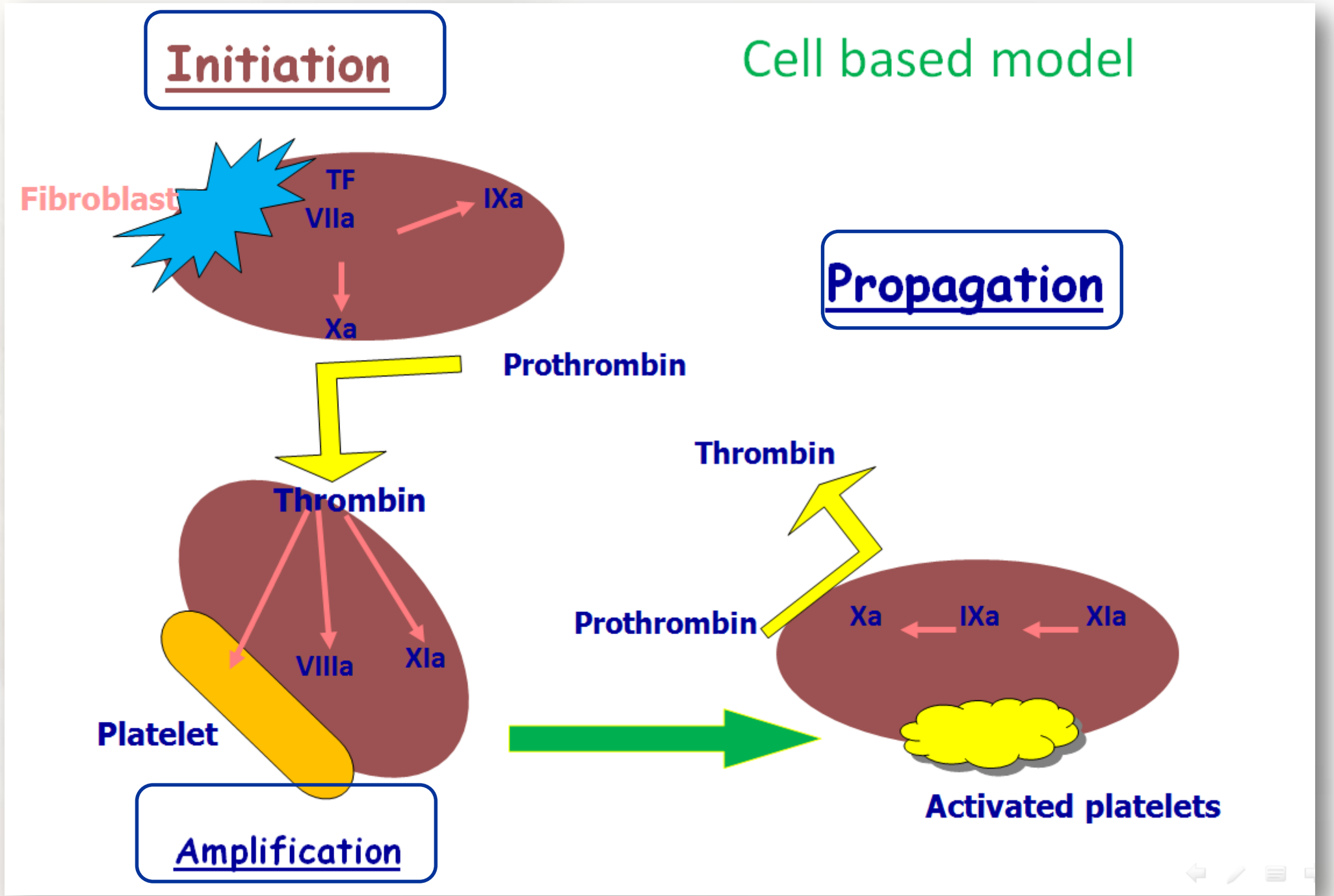
Secretion





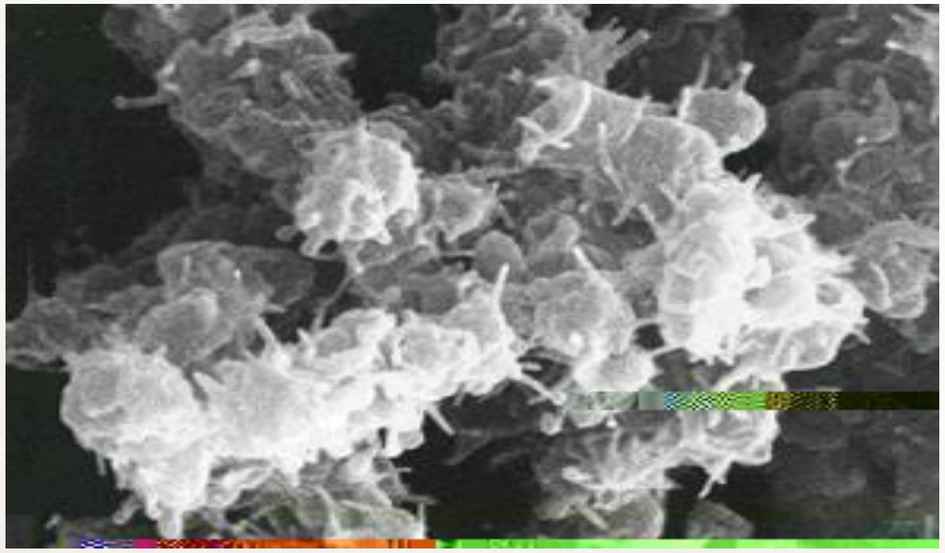


Role of platelet in blood coagulation (The cell based model of blood coagulation) :

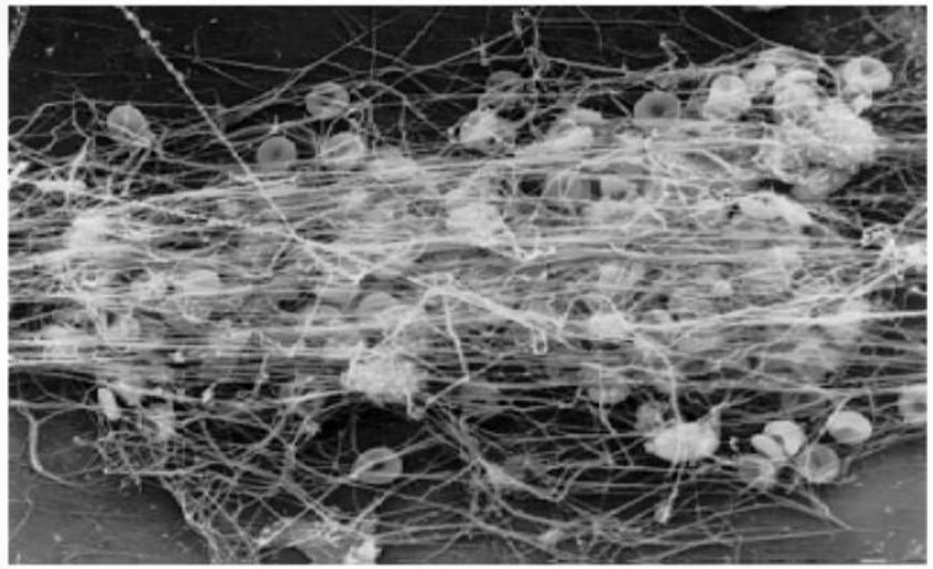


Maintenance of vascular integrity :

Adequate number and function of platelet is essential to participate optimally in haemostasis by :



Initial arrest of bleeding by platelet plug formation



Stabilization of hemostatic plug by contributing to fibrin formation (provide the surface area for formation of fibrin)

with help of Platelet phospholipid (PF3)

http://youtu.be/9QVTHDM90io

Injury

vWf

Extracellular matrix

Adhesion

GPIb-vWf

GPVI-collagen
$\alpha_2\beta_1$-collagen

Activation

Active and recruit other platelets

ADP, TxA_2

Release reaction

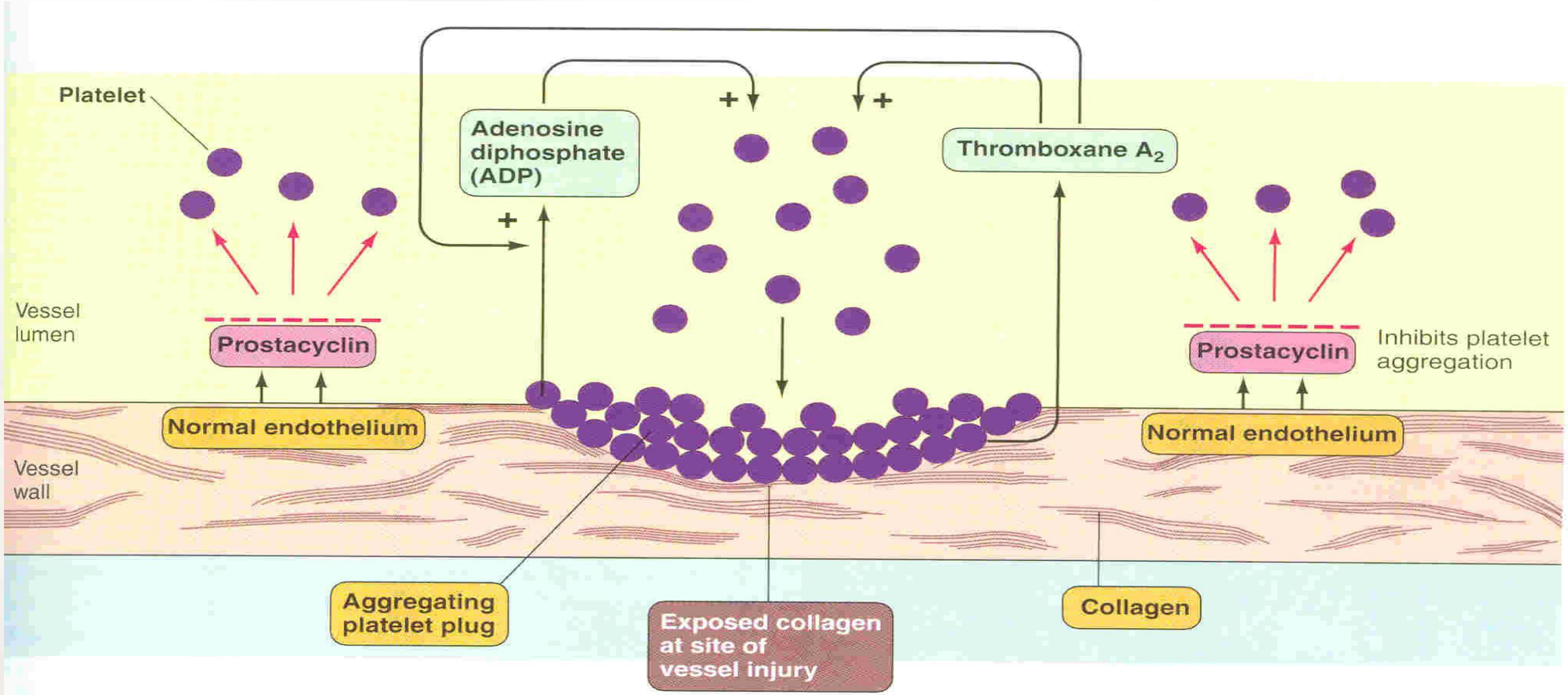
Shape change

Aggregation: Fibrinogen-GPIIb/IIIa

Fibrinogen
GPIIb/IIIa

The primary platelet plug

Platelets aggregation :



The presence of ADB in the blood vessel stimulate the healthy endothelial to produce prostacyclin & nitric-oxide to inhibit platelets aggregation and relax the muscles all over the uninjured blood vessels

Bleeding Disorders

1)Bleeding can result

- deficiency in **number** of the Platelet
  - Also called **thrombocytopenia**
- defect in **function** of the Platelet *

2)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 disorders
  - Thrombocytopenia with absent radii (TAR)
    - Paris-Trousseau/Jacobsen

*Normal count but the function is abnormal due to congenital disorder or due to drug like if we take aspirin we will develop bleeding because aspirin block TXA2

Bleeding Disorders

2)Congenital Platelet Disorders

Disorders of Adhesion

Bernard-Soulier

hemorrhagiparous thrombocytic dystrophy,[is a rare **autosomal recessive coagulopathy** (bleeding disorder)

that causes a **deficiency of *glycoprotein Ib* (GpIb), the receptor for von Willebrand factor**, an important glycoprotein involved in hemostasis.

Disorder of Aggregation:

. Glanzmann thrombosthenia

bnormality of platelets.

in which the platelets contain defective or low levels of glycoprotein IIb/IIIa (GpIIb/IIIa), which is a receptor for fibrinogen. As a result, no fibrinogen bridging of platelets to other platelets can occur, and the **bleeding time is significantly prolonged**

Laboratory Testing of Platelet Functions

- Platelet Aggregation
- Electron-microscopy
- Platelet count & shape
- Flow-cytometry
- Platelet Function Analyzer
- Bleeding time
- Granule release products

The laboratory specialist will look at how the platelets spread out in the liquid part of the blood (plasma) and whether they form clumps after a certain chemical or drug is added. When platelets clump together, the blood sample is more clear. A machine measures the changes in cloudiness and prints a record of the results

in (PRP) Platelet rich plasma):
Provides information on time course of plat. activation.

Agonists:
ADP
Adrenaline
Collagen
Arachidonic acid
Ristocetin
Thrombin

These substance must be added to the plasma to stimulate aggregation

platelet disorder investigation

Laboratory Testing of Platelet Functions

- Platelet Aggregation
- Electron-microscopy
- Platelet count & shape
- Flow-cytometry
- Platelet Function Analyzer
- **Bleeding time**
- Granule release products

Bleeding time is a medical test done on someone to assess their platelet function It involves making a patient bleed then timing how long it takes for them to stop bleeding

Summary for 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

Platelets secretion

- 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

@PhysiologyTeam

Pht433@gmail.com

Physiology team

Done by :

Rahma Alshehri

Raneem Alotaibi

Rahaf Altwijri

Revised by :

Muhannad Alwabel

GOOD LUCK