بسم الله الرحمن الرحيم

Platelet Structure & Function

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Objectives

-- Understand platelet normal ultrastructure

-- Understand the functions of different platelets organelles and surface receptors

-- Understand the mechanisms of platelet functions

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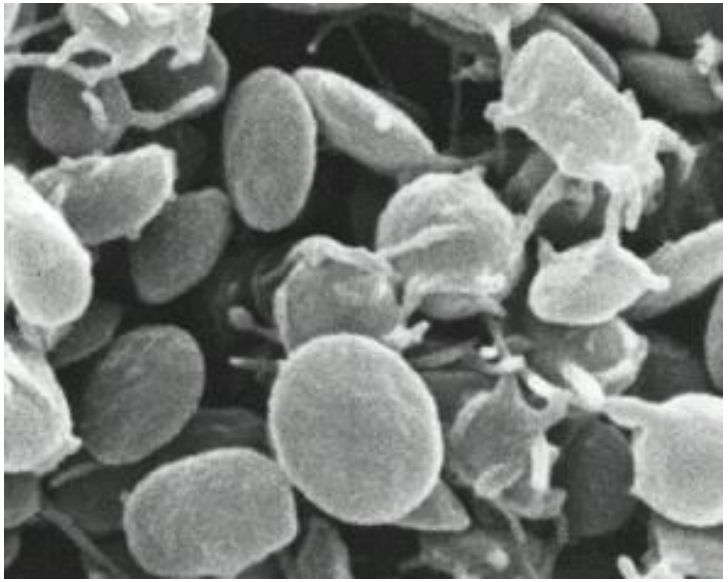
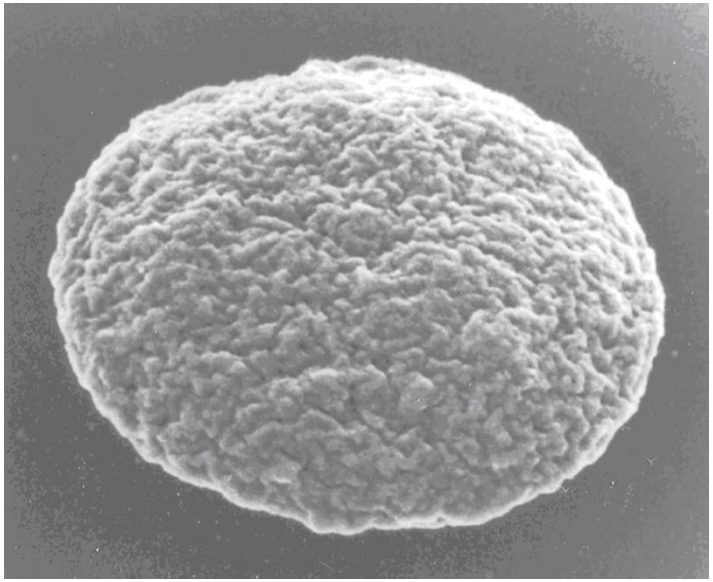
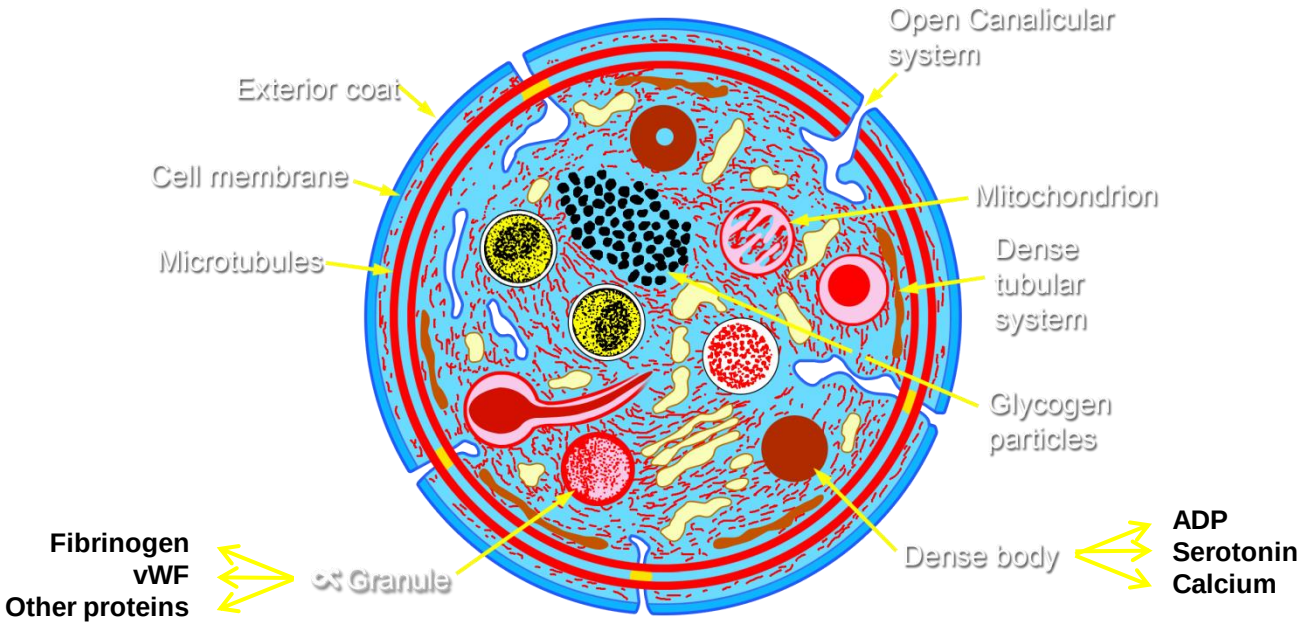
- Relate membrane receptors and granule content to normal function in hemostasis and bleeding (platelet) disorders

Platelet ultra-structure



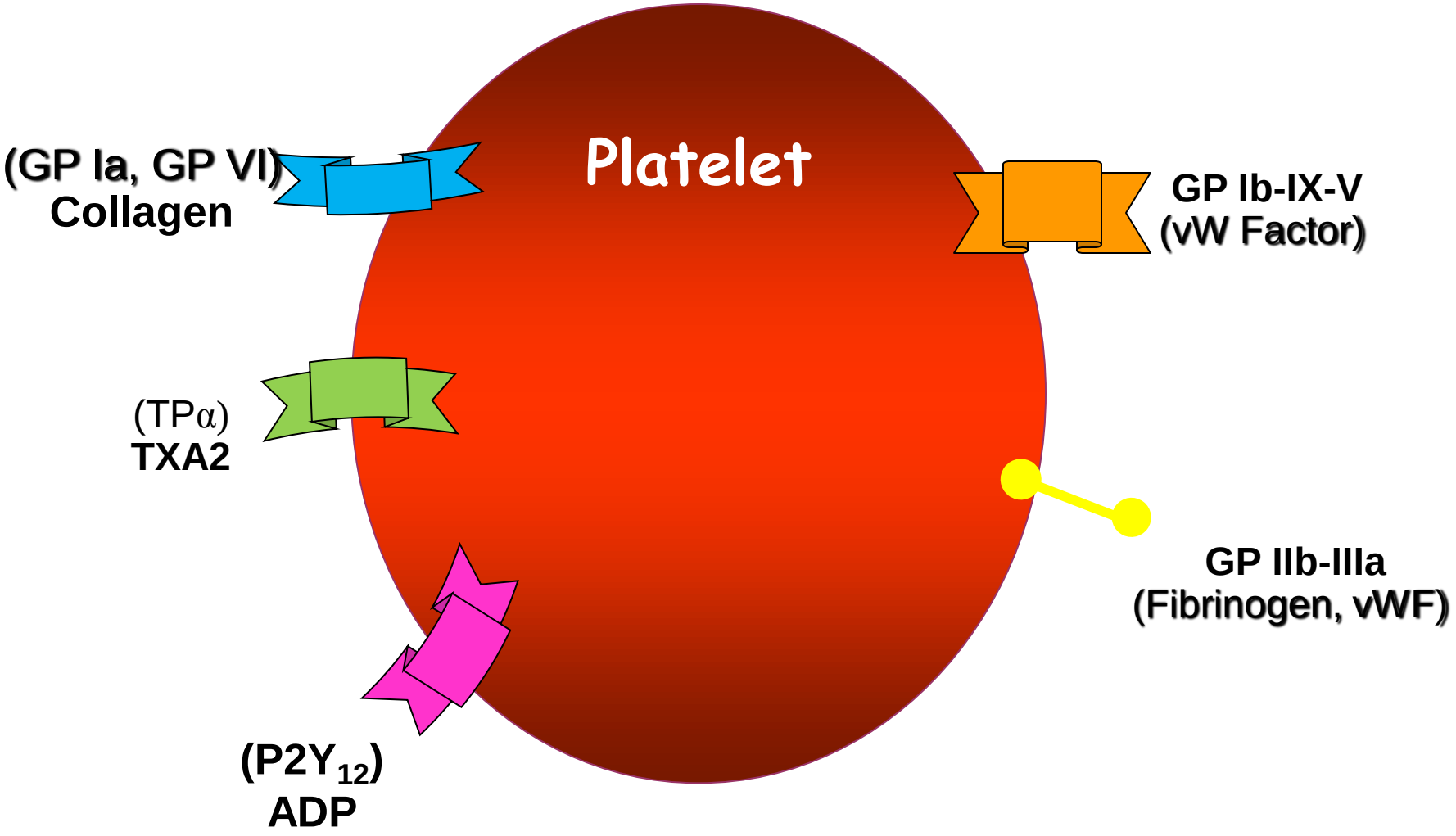


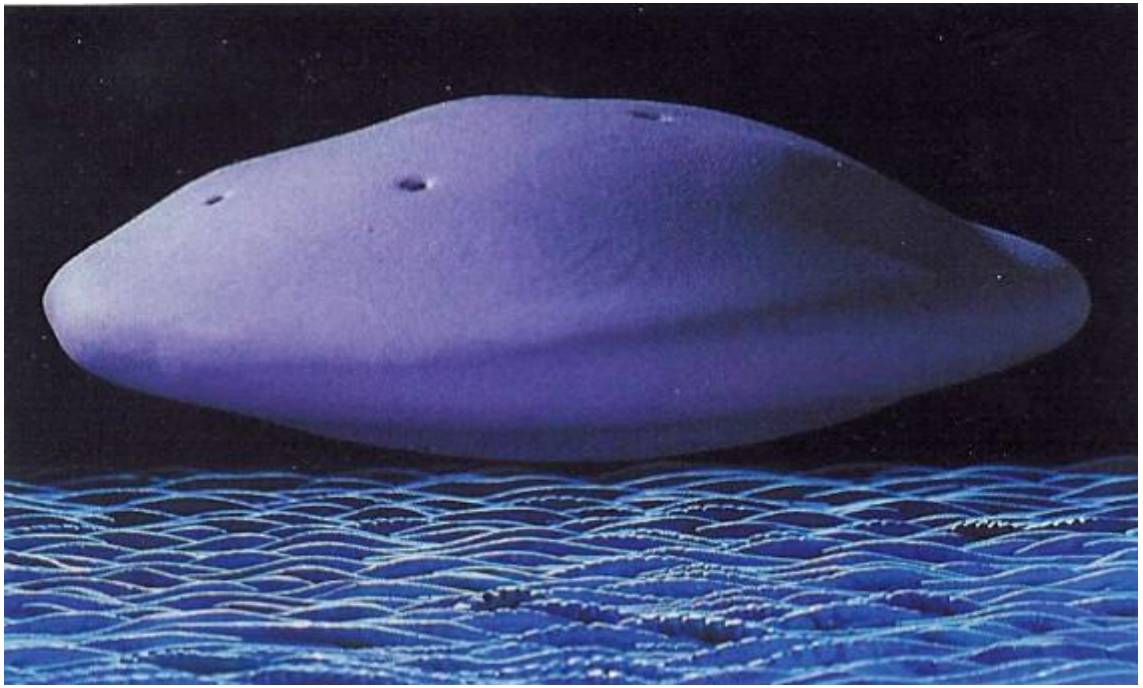

Open Canalicular system
Exterior coat
Cell membrane
Mitochondrion
Microtubules
Dense tubular system
Glycogen particles
Fibrinogen
vWF
Other proteins
α Granule
Dense body
ADP
Serotonin
Calcium

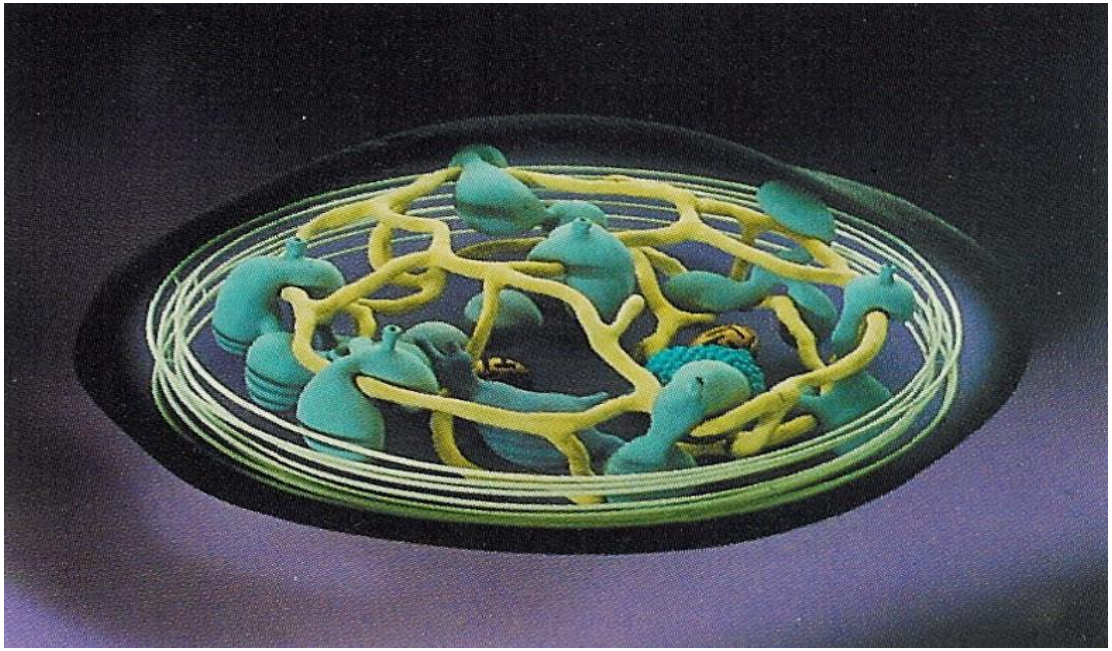
(Thrombocytes)

- Anuclear and discoic cell → spherical when activated
- Platelet count = 150 $x10^3$-300$x10^3$/ml
- Size: 1.5–3.0 μm
- Life span: 7–10 days
- Sequestered in the spleen; hypersplenisın may lead to low platelet counts.

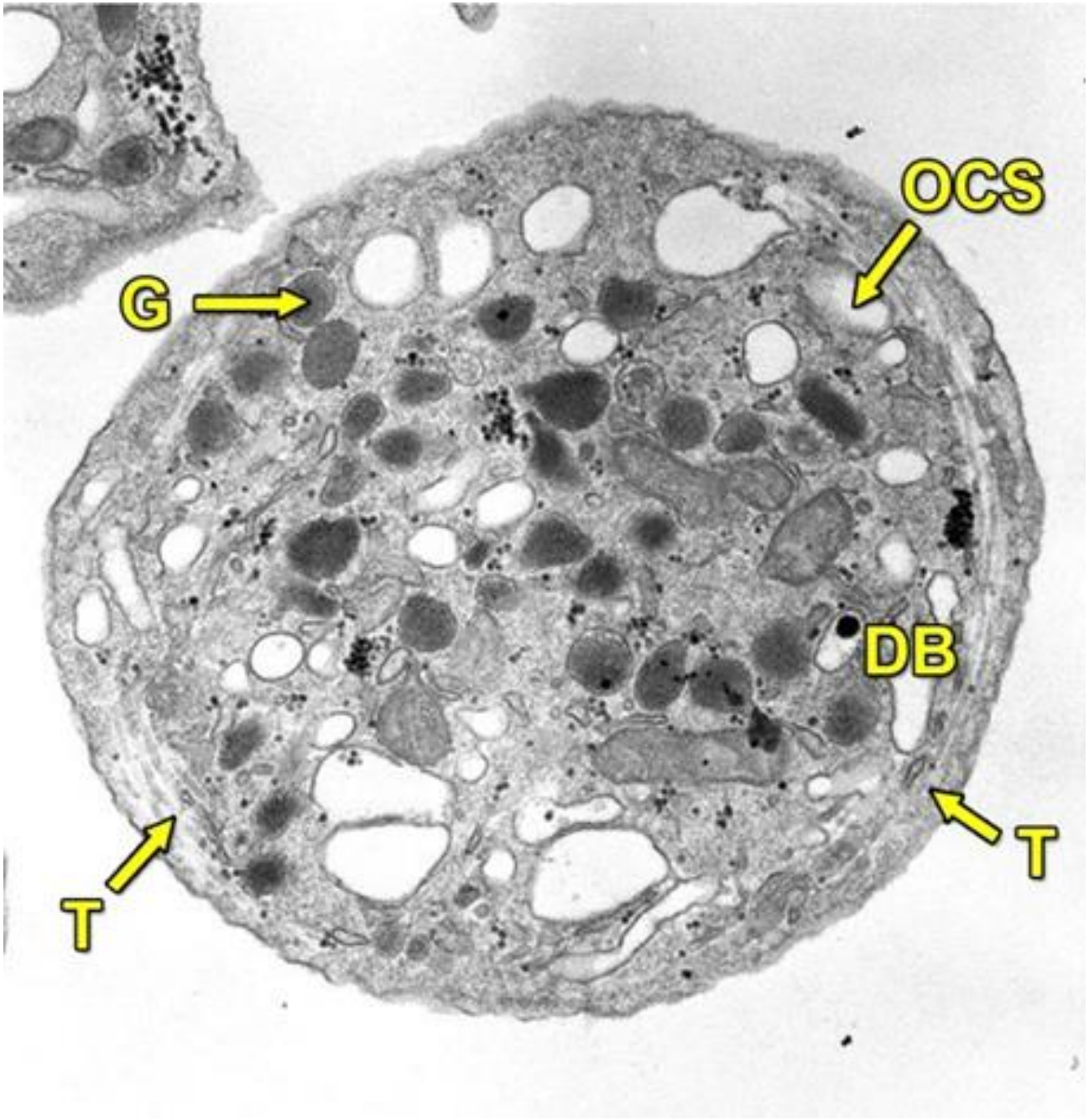
Platelet Receptors







Platelet EM


OCS
G
DB
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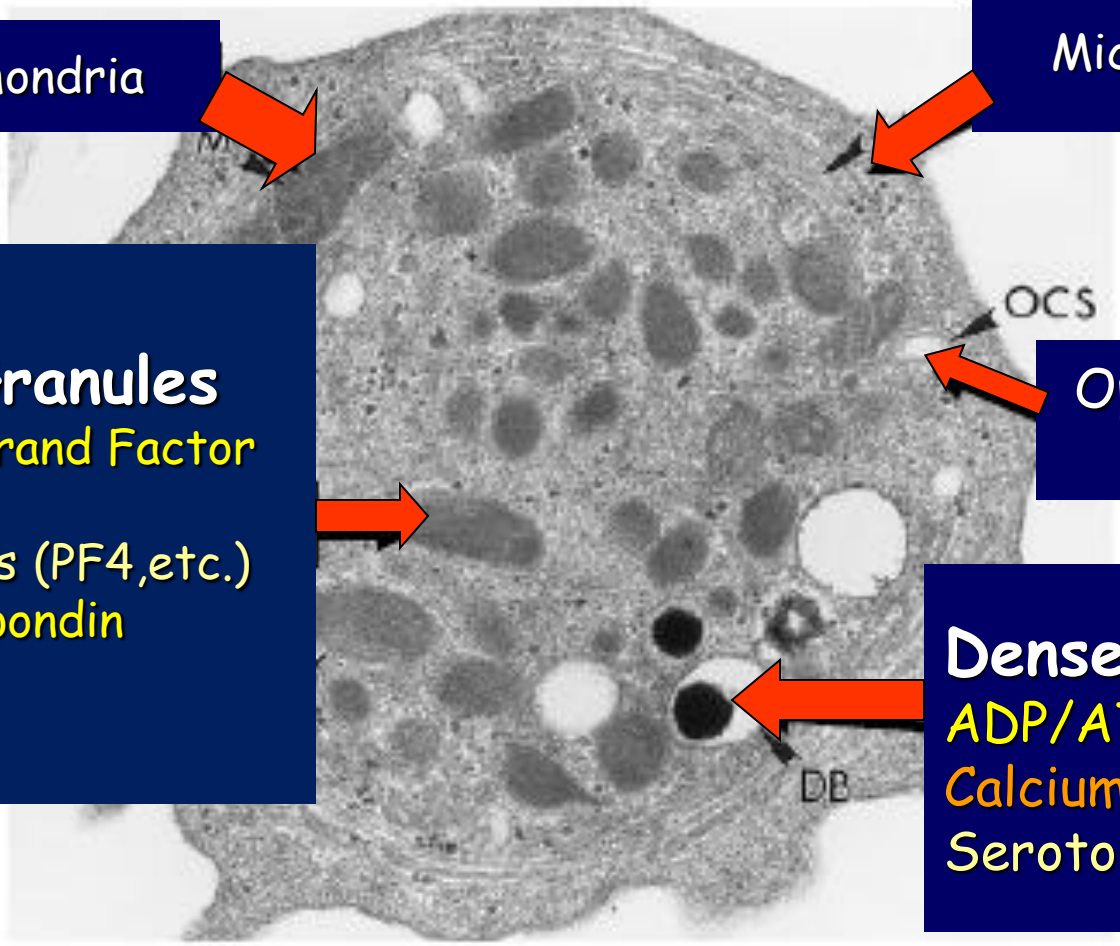
Platelet Ultrastructure

Mitochondria

Microtubules



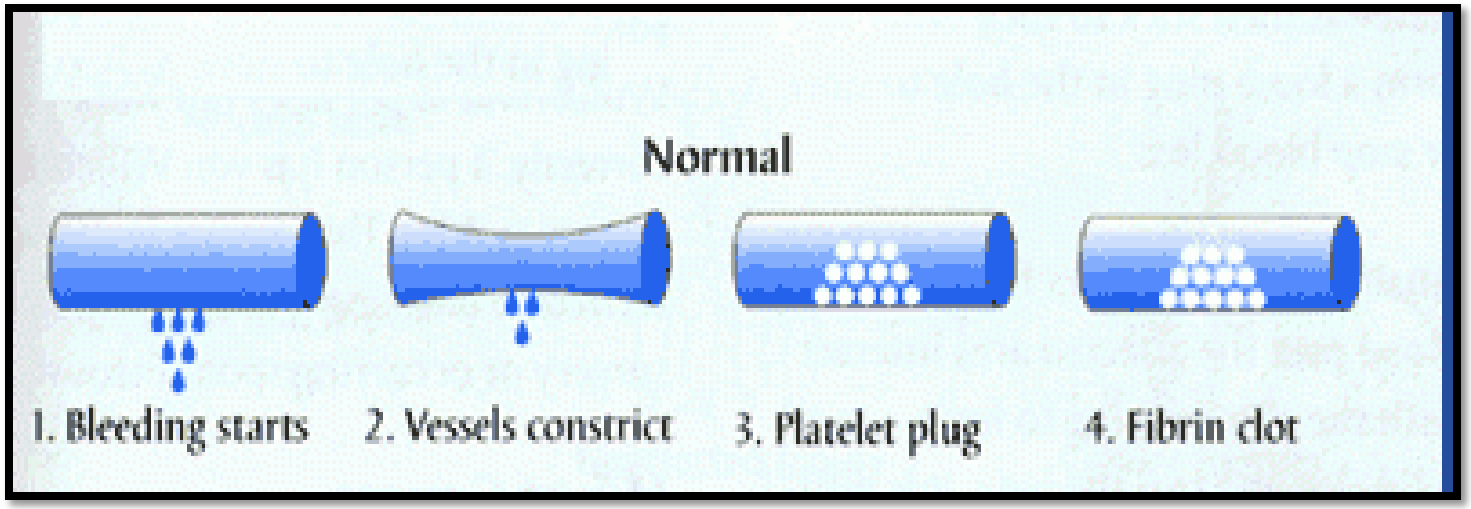
Alpha Granules
von Willebrand Factor
Fibrinogen
Chemokines (PF4,etc.)
Thrombospondin
P-selectin

Open canalicular system

Dense Granules
ADP/ATP
Calcium
Serotonin

General functions of the platelets

HEMOSTASIS



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

Hemostatic Mechanisms

1. Vessel wall
2. Platelet
3. Blood coagulation
4. Fibrinolytic system

Platelet activation:

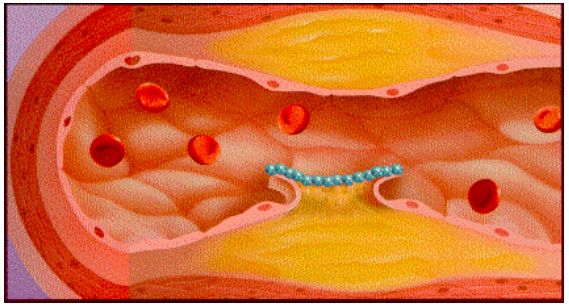
1. Adhesion
2. Shape change
3. Aggregation
4. Release reaction
5. Clot retraction

https://www.youtube.com/watch?v=0pnpoEy0eYE

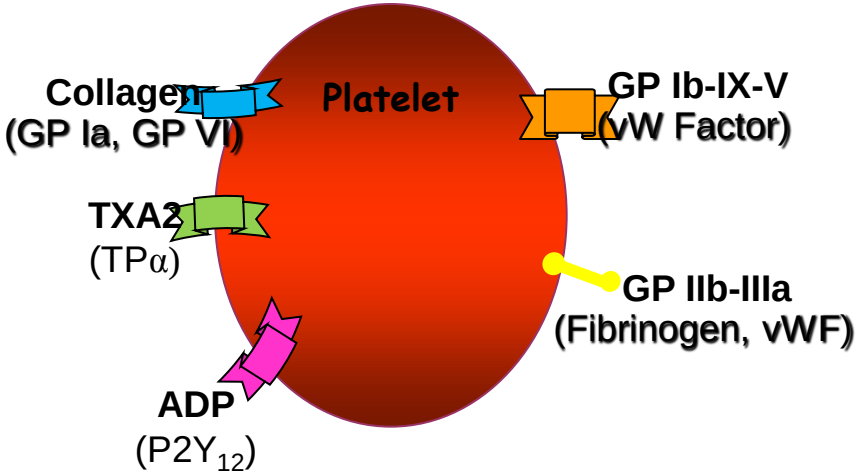
Platelet Activation

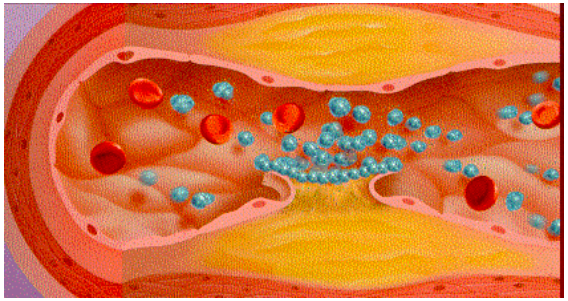
- Adhesion
- Aggregation
- Release
- Clot Retraction

Platelet function

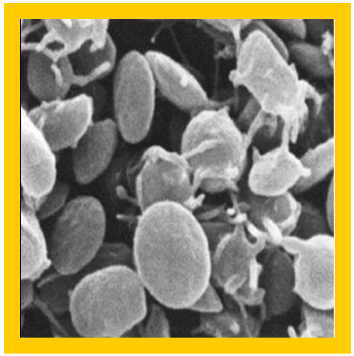


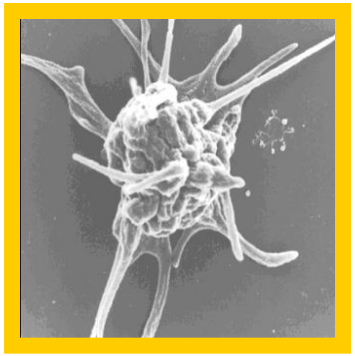
Adhesion

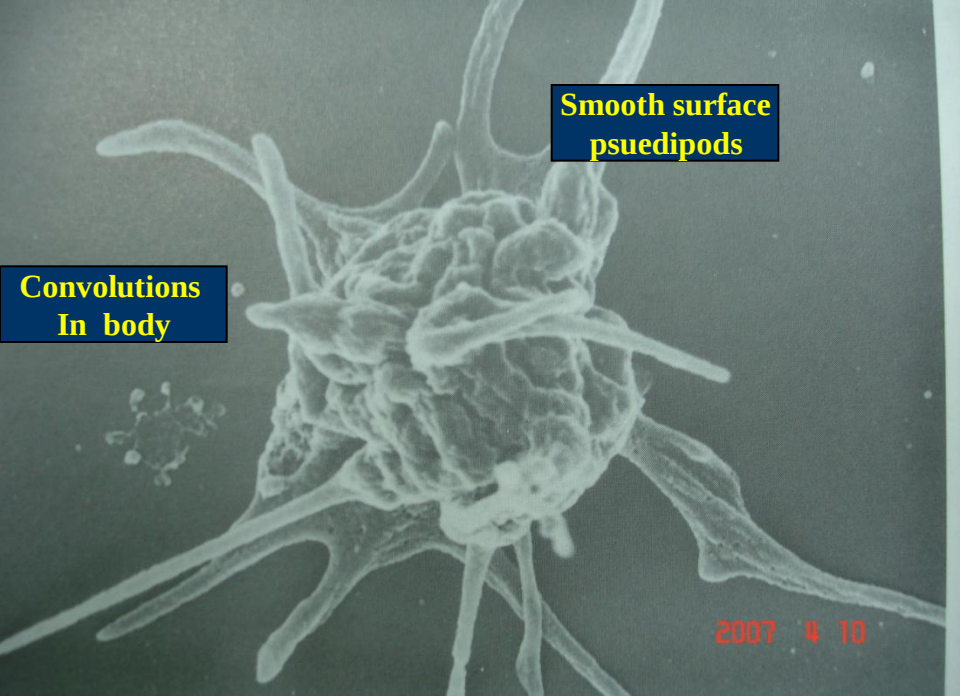


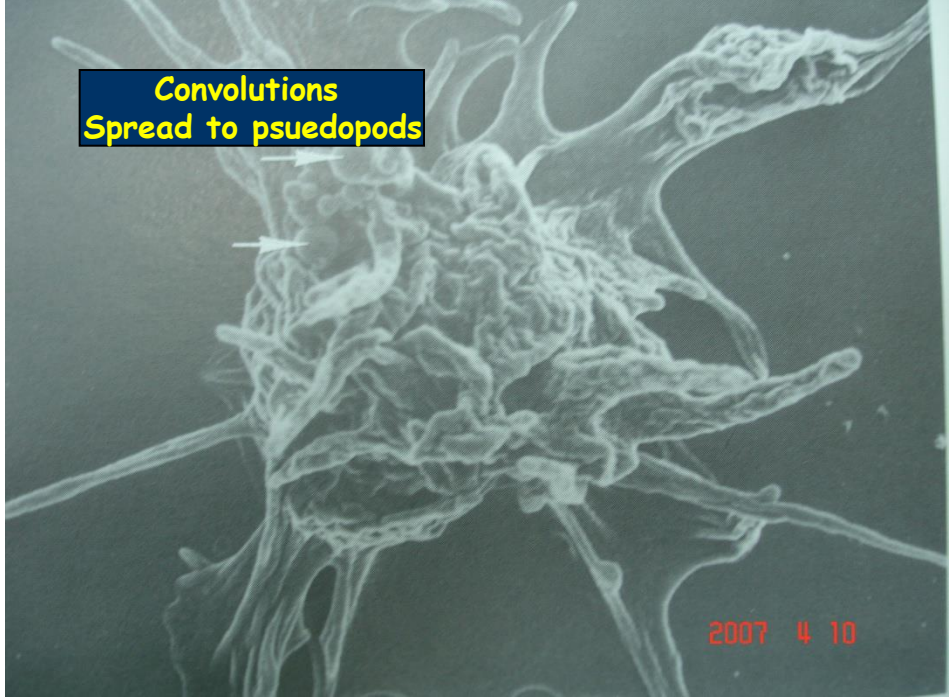


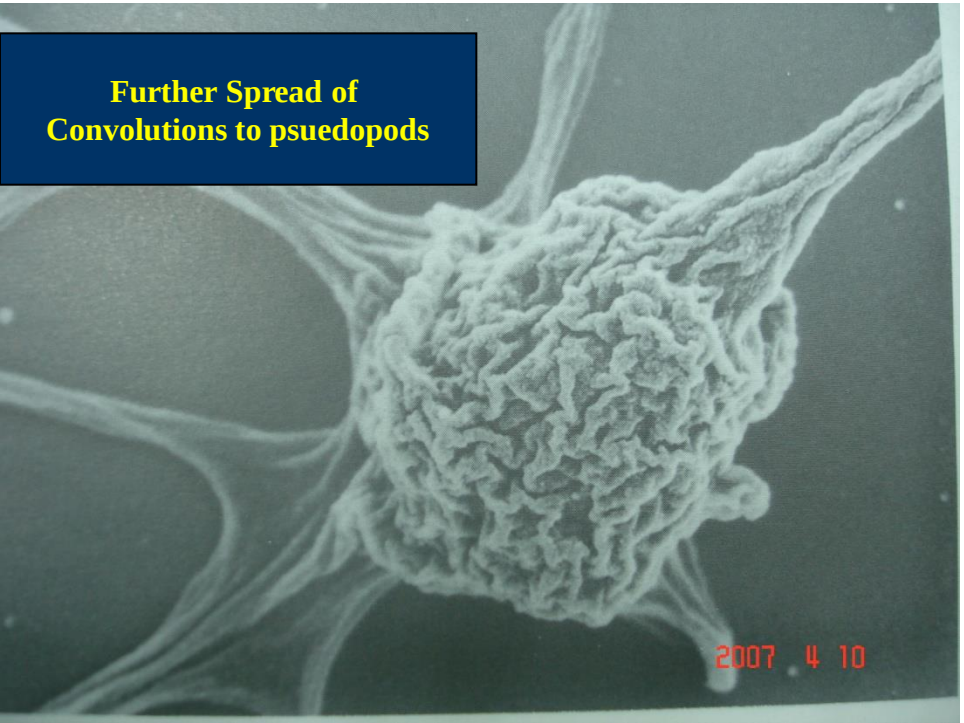
Activation

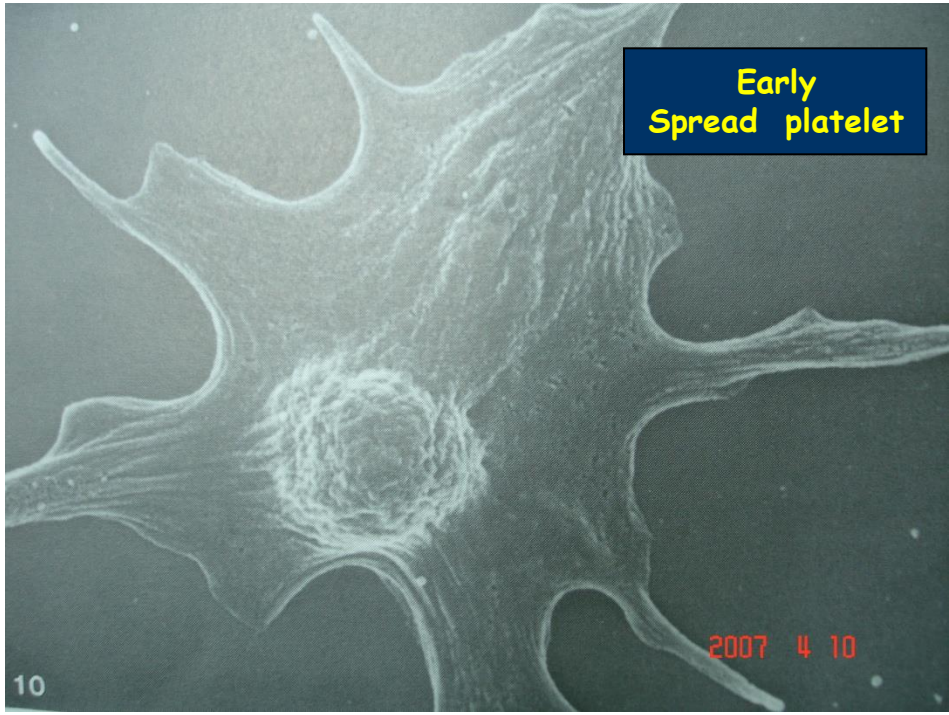





Smooth surface
psuedipods
Convolutions
In body
2007 4 10


Convolutions
Spread to psuedopods
2007 4 10


Further Spread of
Convolutions to psuedopods
2007 4 10

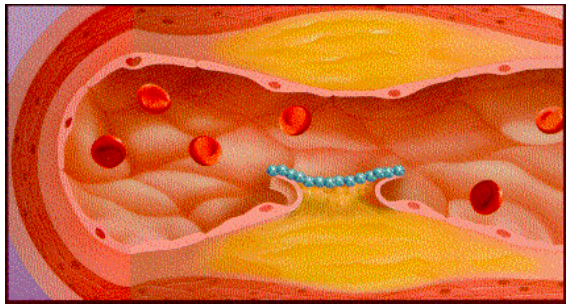

Early
Spread platelet
2007 4 10
10

Platelet Aggregation

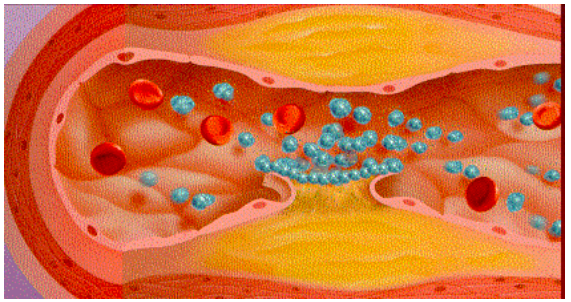
- **Aggregation:**

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

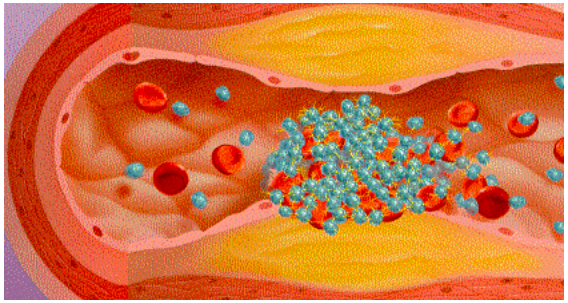
Platelet function



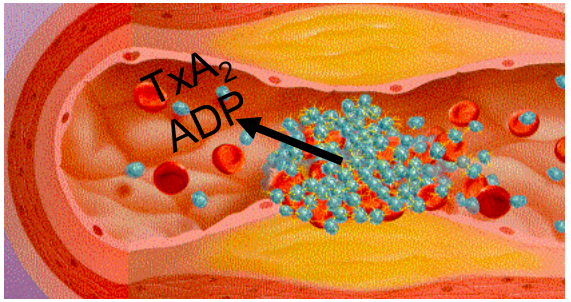
Adhesion



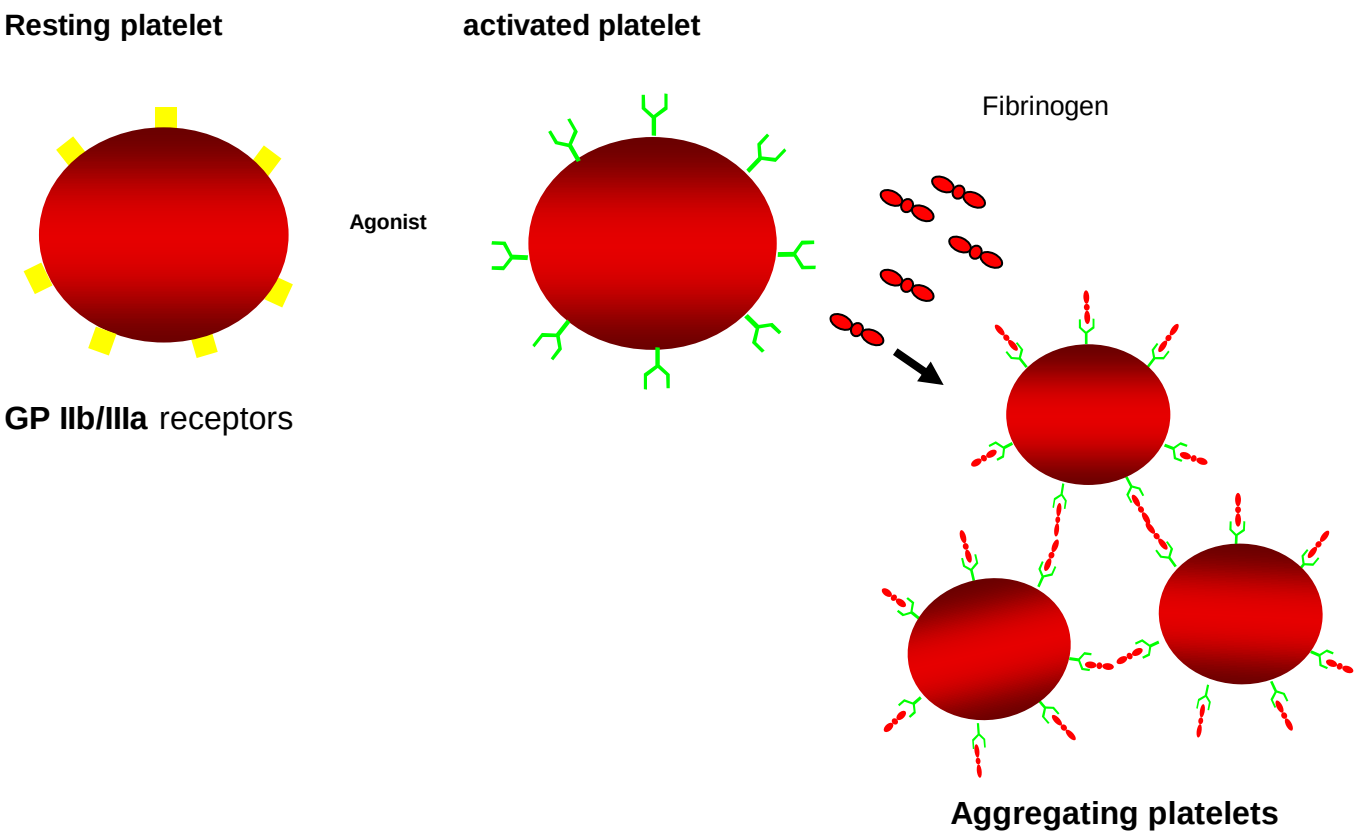
Activation



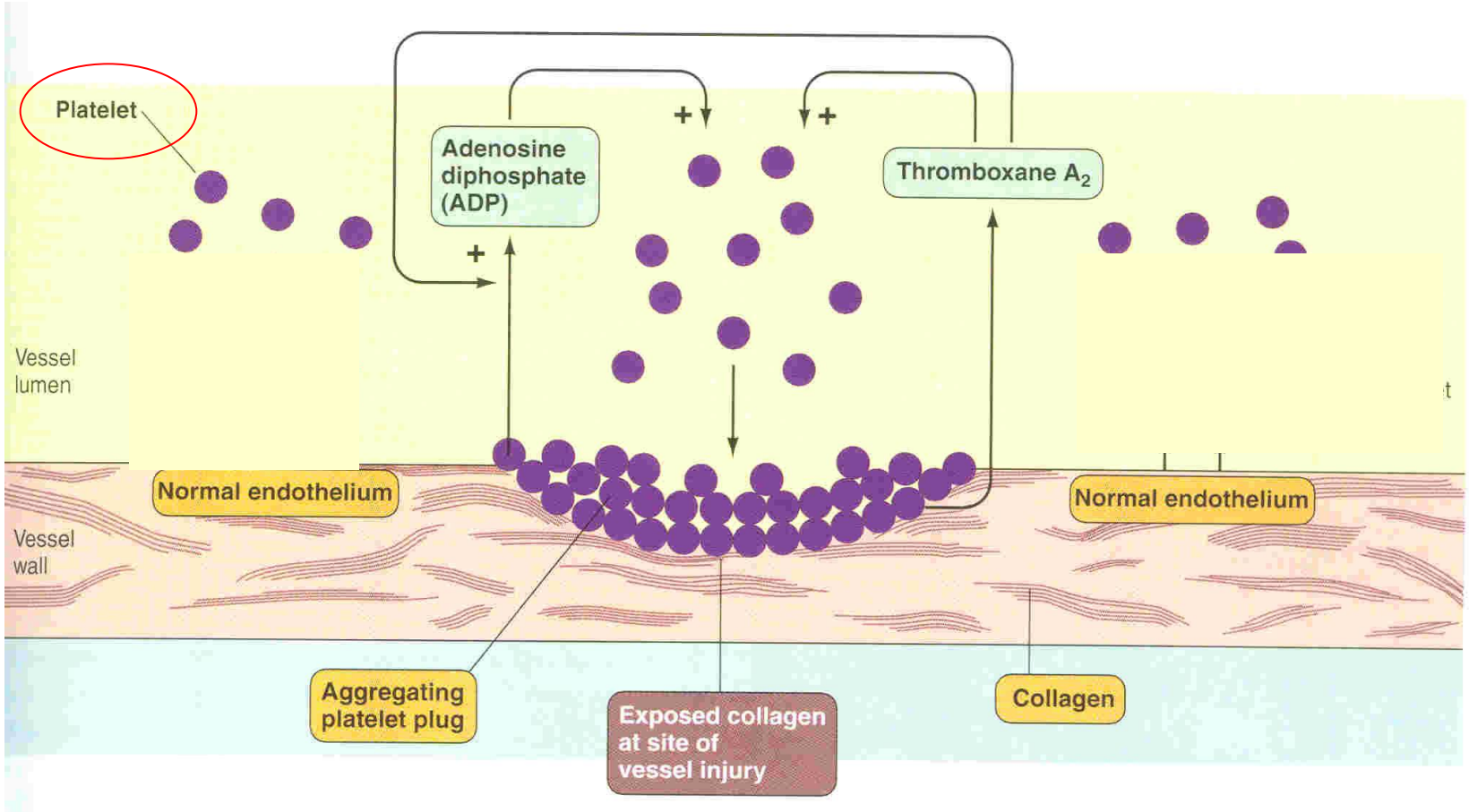
Aggregation

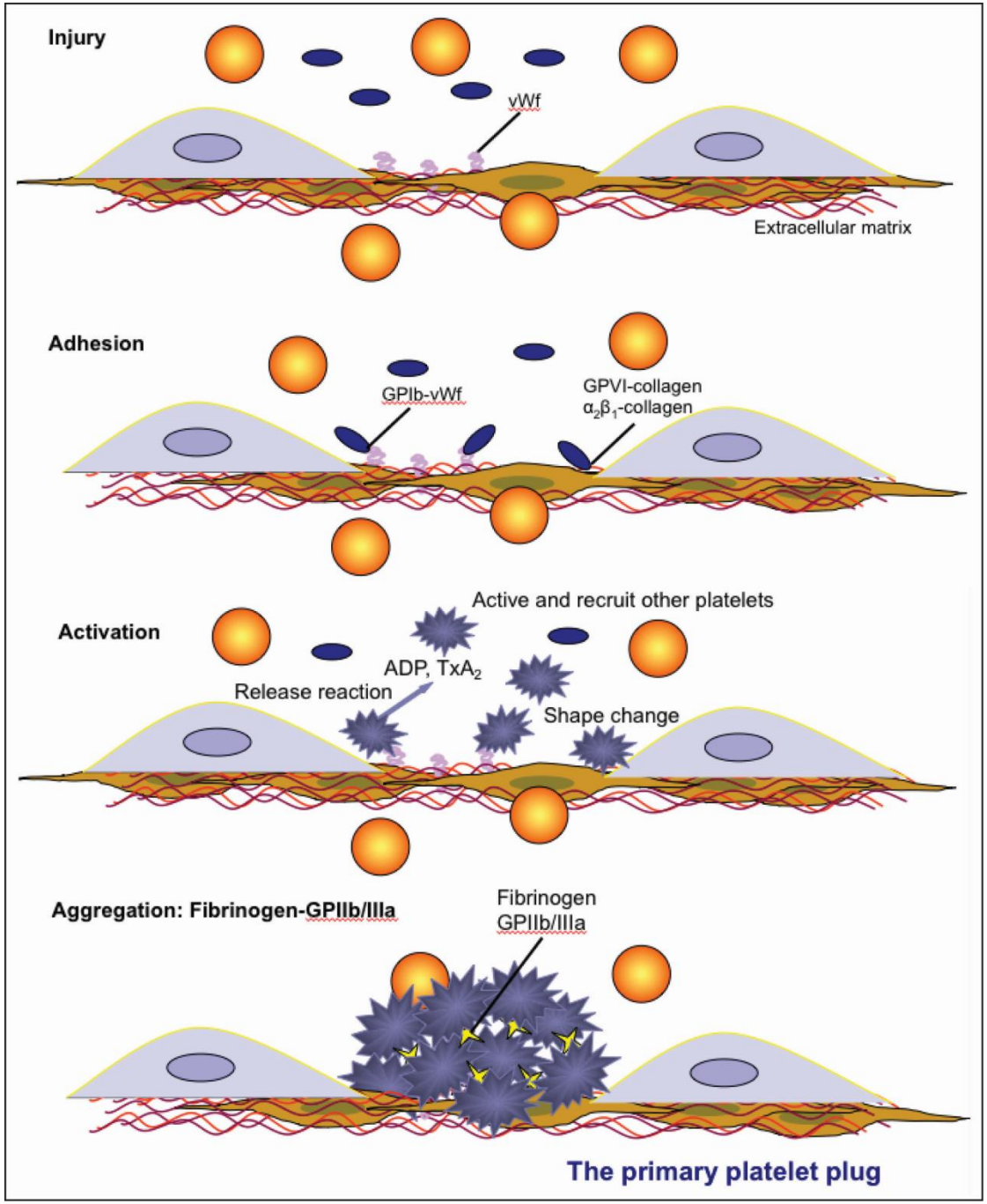


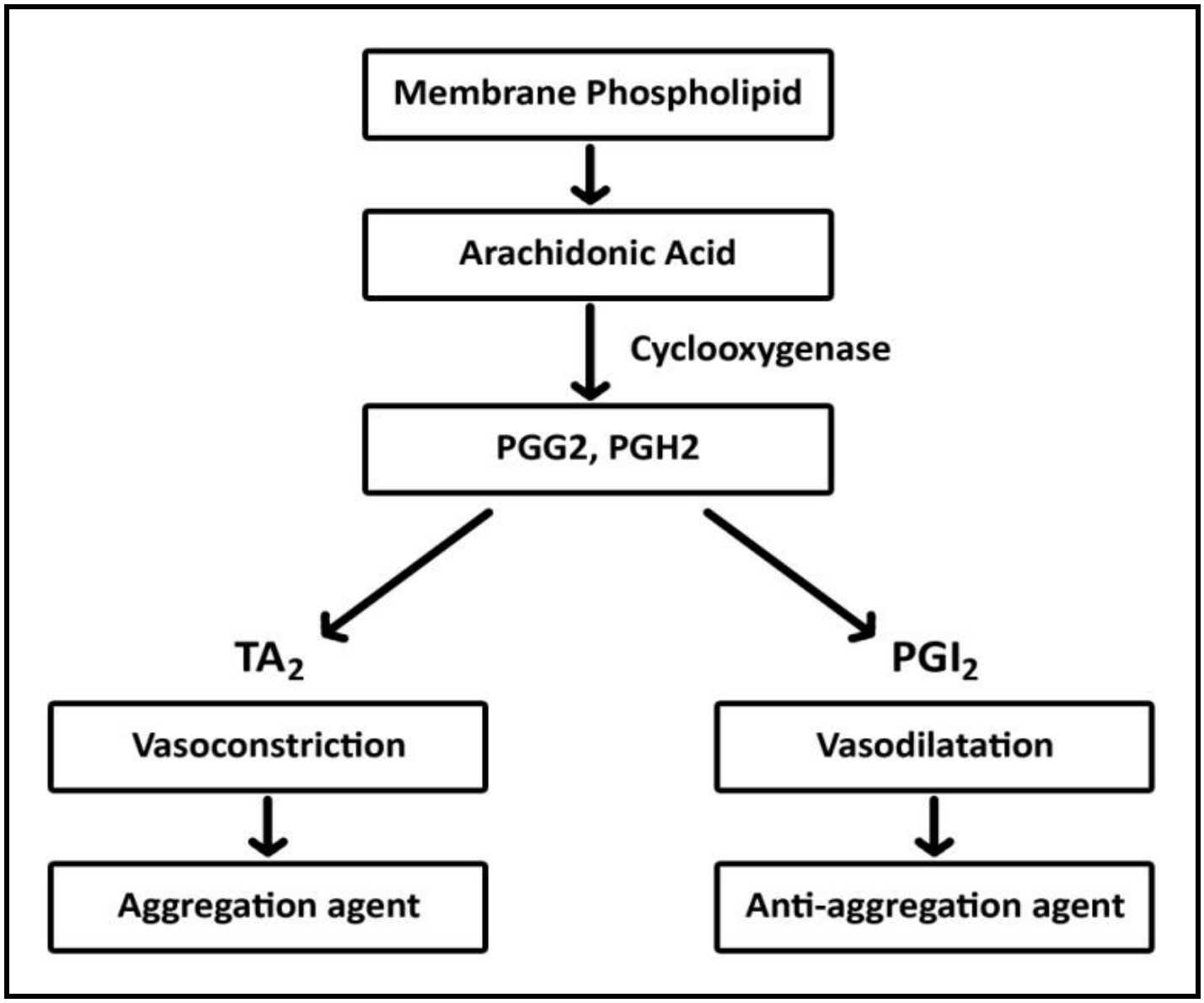
Secretion


Resting platelet
activated platelet
Agonist
Fibrinogen
GP IIb/IIIa receptors
Aggregating platelets

Platelets aggregation




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


Membrane Phospholipid
Arachidonic Acid
Cyclooxygenase
PGG2, PGH2
TA2
PGI2
Vasoconstriction
Vasodilatation
Aggregation agent
Anti-aggregation agent

Activated Platelets

Secrete:

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

   Function:

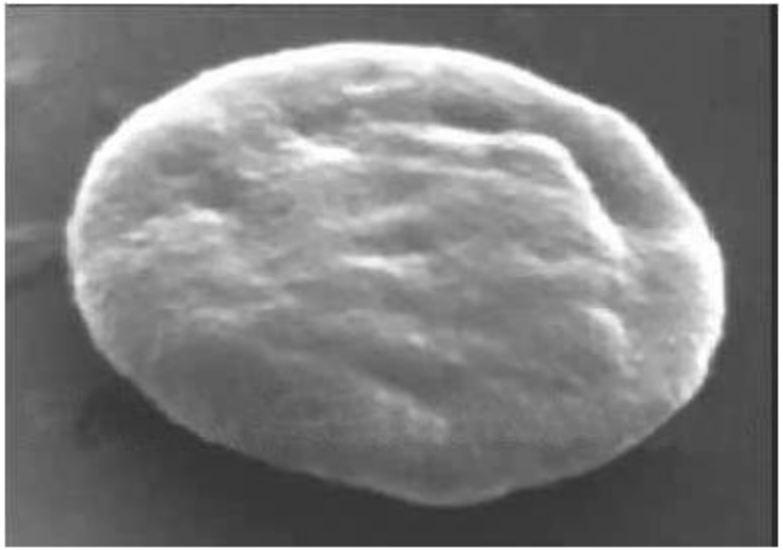
- vasoconstriction
- Platelet aggregation

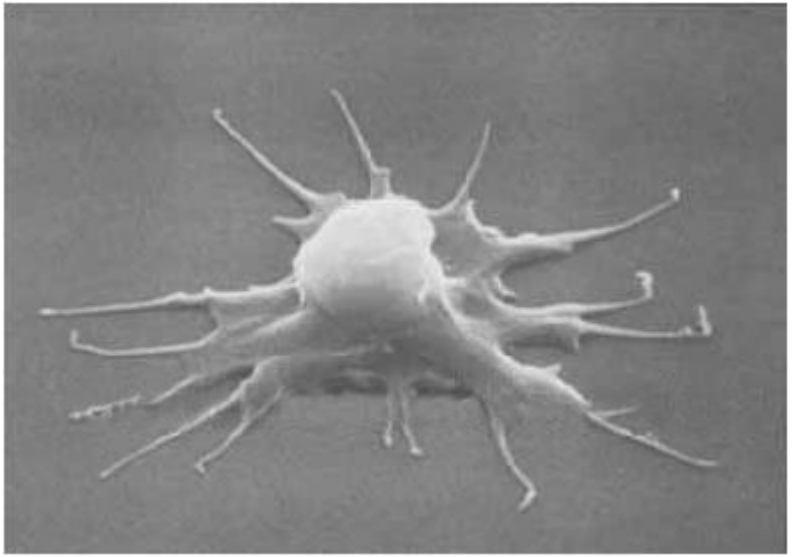
  (TXA2 inhibited by aspirin)

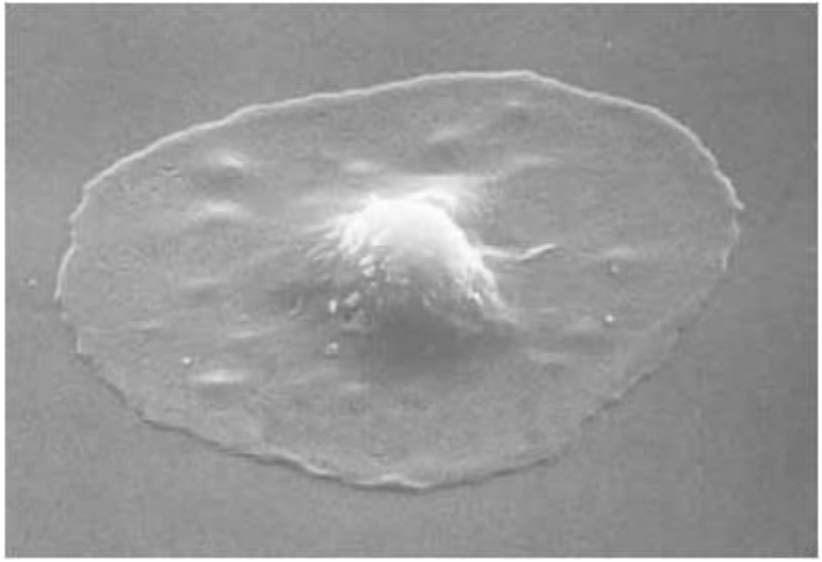
Platelet Activation

- **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

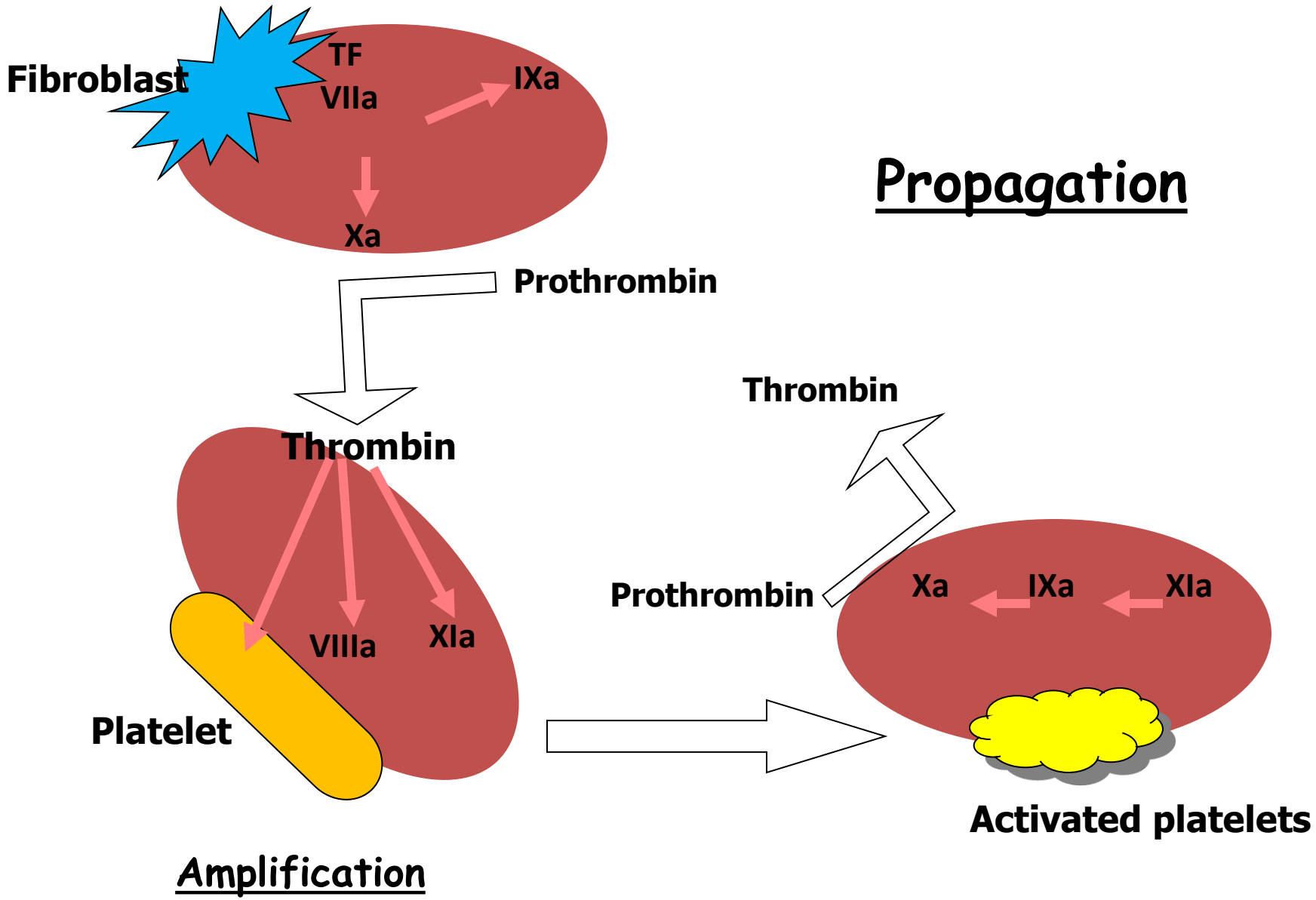
- Platelets activated by adhesion
- Extend projections to make contact with each other
- Release:
  thromboxane A2, serotonin & ADP >>> activating other platelets
- Serotonin & thromboxane A2 are **vasoconstrictors** decreasing blood flow through the injured vessel.
- ADP causes stickiness and enhances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

Functions of the platelets..cont

Role of platelet in blood coagulation

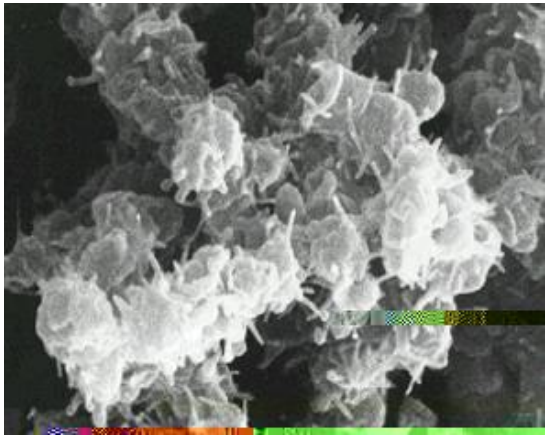
(The cell based model of blood coagulation)

Cell based model

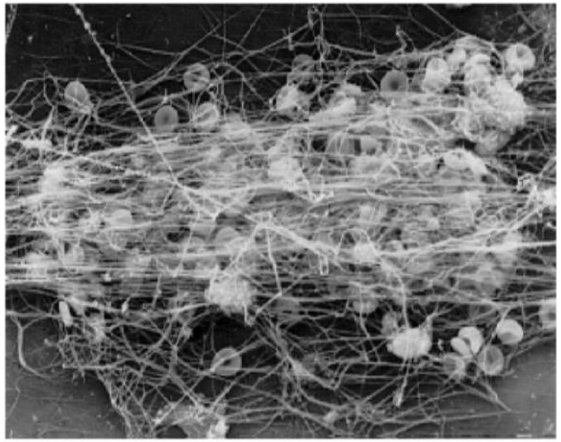


Platelet function:
Maintenance of vascular integrity

- Initial arrest of bleeding by platelet plug formation

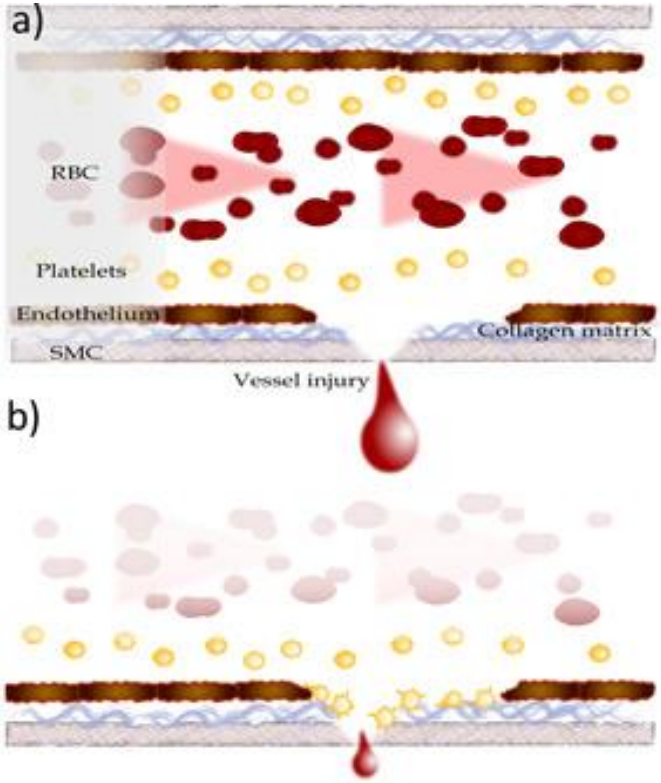


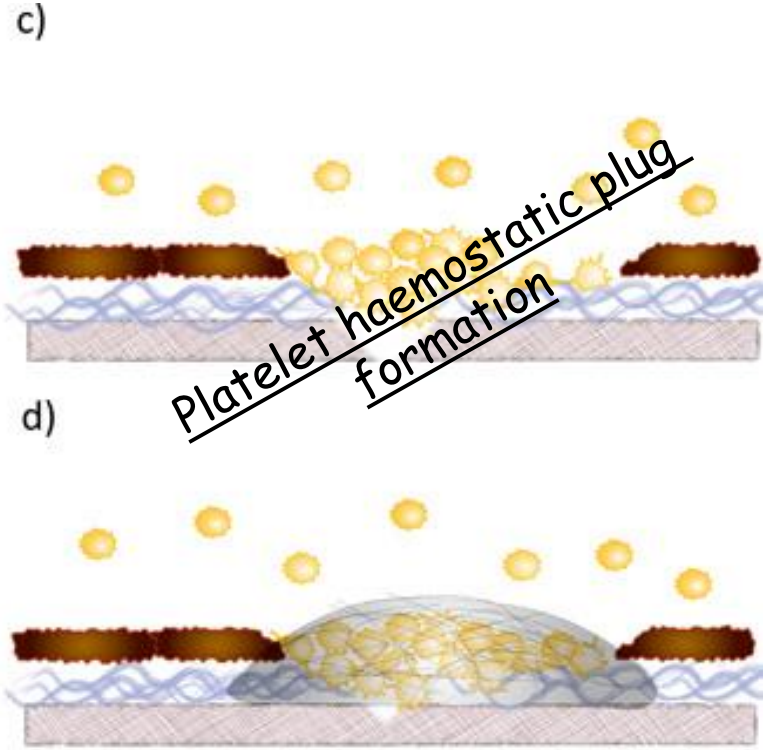
- Stabilization of hemostatic plug by contributing to fibrin formation



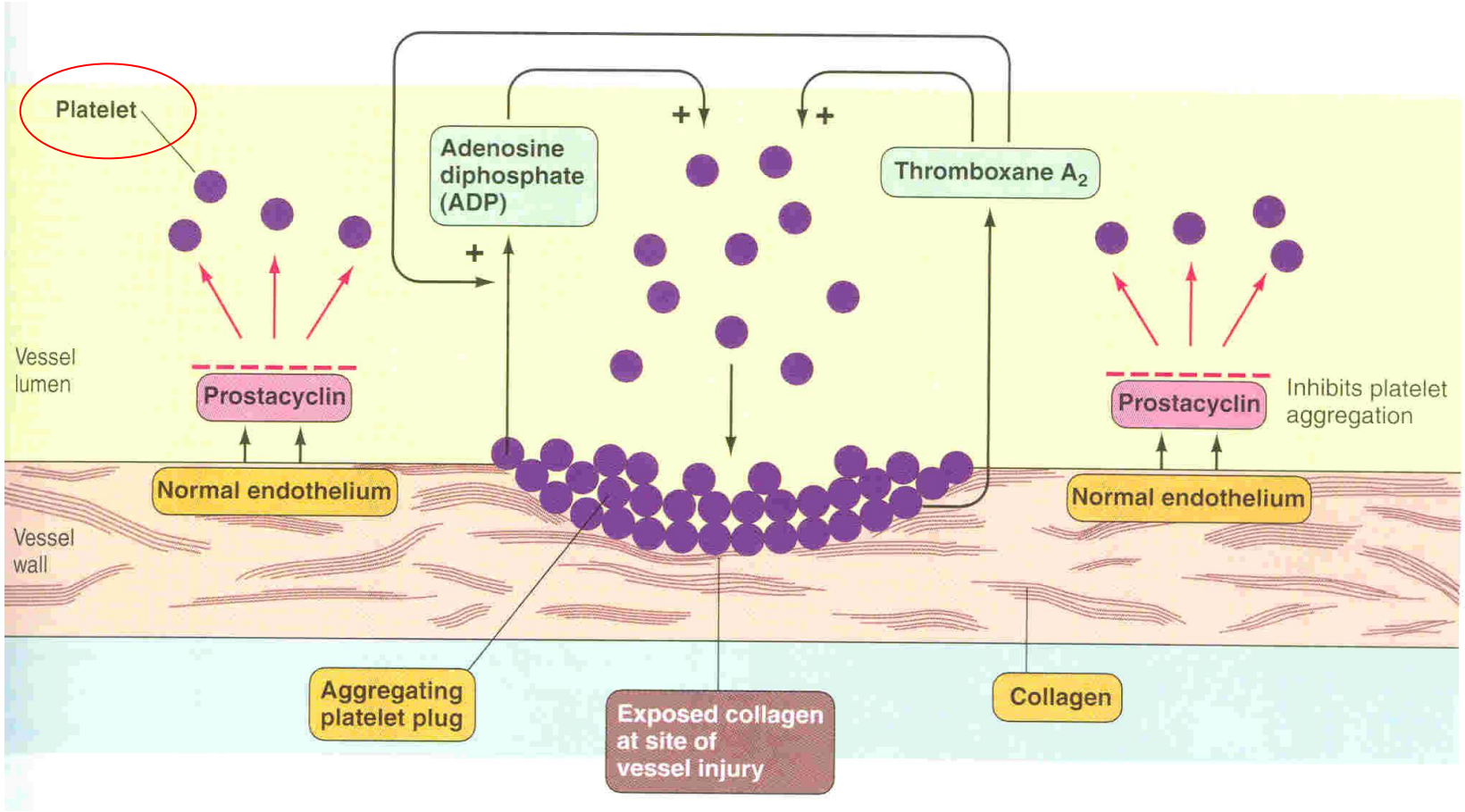
Adequate number and function of platelet is essential to participate optimally in haemostasis

Platelet haemostatic plug formation





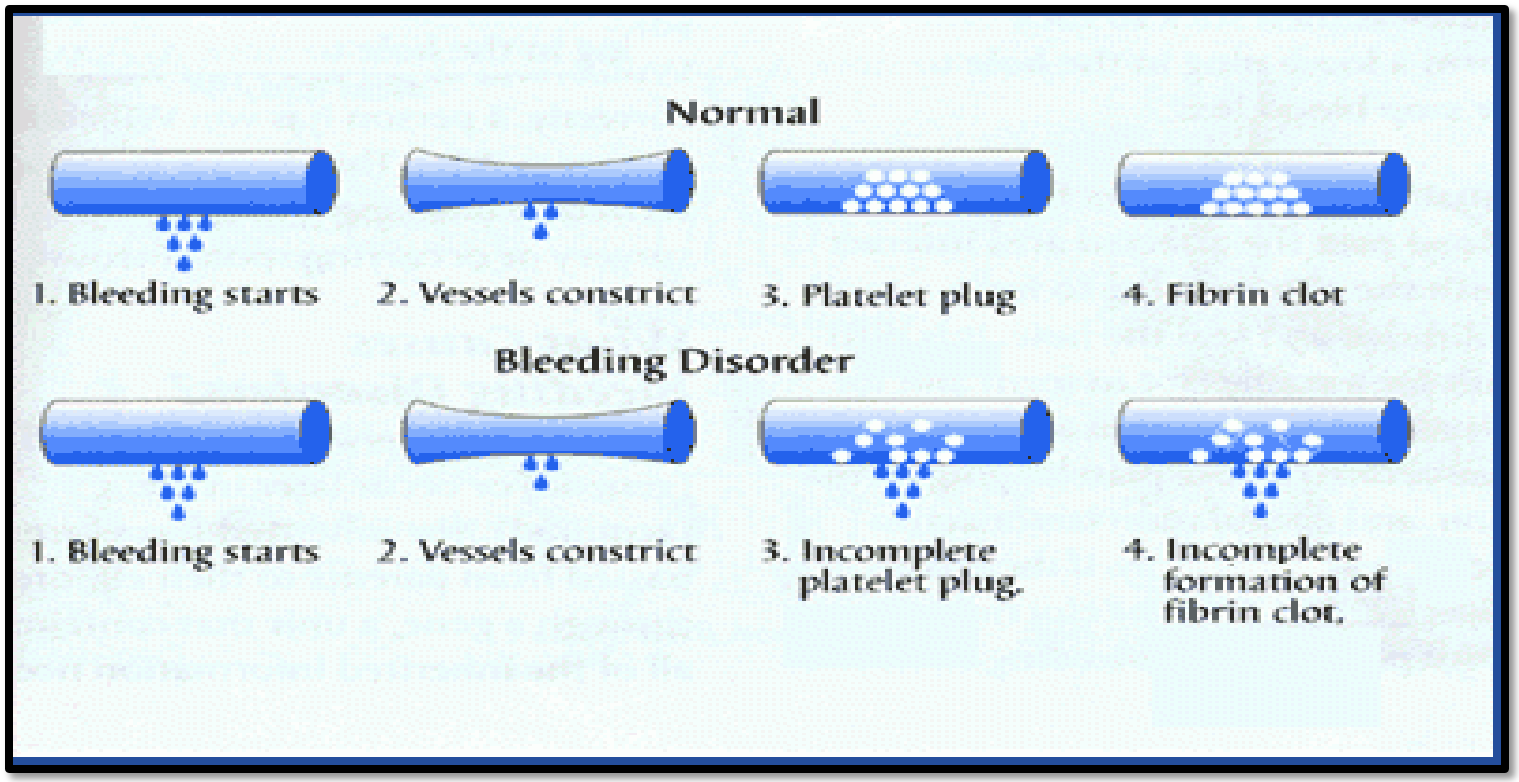
Platelets aggregation



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 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 and von Willebrand factor (vWF)**

Bleeding Disorders



- **Bleeding can result from:**
  - **Platelet defects:**

    deficiency in number (thrombocytopenia)

    defect in function.

(Thrombocytopenia)

The causes of decreased platelet counts are:

• **Decreased Production**

Leukemia or lymphoma
Cancer treatments such as radiation or chemotherapy
Various anemias
Toxic chemicals
Medications: diuretics, chloramphenicol
Viruses: chickenpox, mumps, Epstein-Barr, parvovirus, AIDS
Alcohol in excess
Genetic conditions: Wiskott-Aldrich, May-Hegglin,

• **Abnormal distribution**

Splenomegaly with sequestration in the spleen

• **Increased destruction**

Autoimmune diseases: Idiopathic (immune) thrombocytopenic purpura
Medications: quinine, antibiotics containing sulfa, Dilantin®, vancomycin,
rifampin, heparin-induced thrombocytopenia
Surgery: man-made heart valves, blood vessel grafts, bypass machines
Infection: septicemia
Pregnancy: about 5% of pregnant women develop mild decrease Thrombotic thrombocytopenic purpura
Disseminated intravascular coagulation

• Pseudothrombocytopenia

Partial clotting of specimen
EDTA-platelet clumping
Platelet satellitism around WBCs
Cold agglutinins
Giant platelets

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)

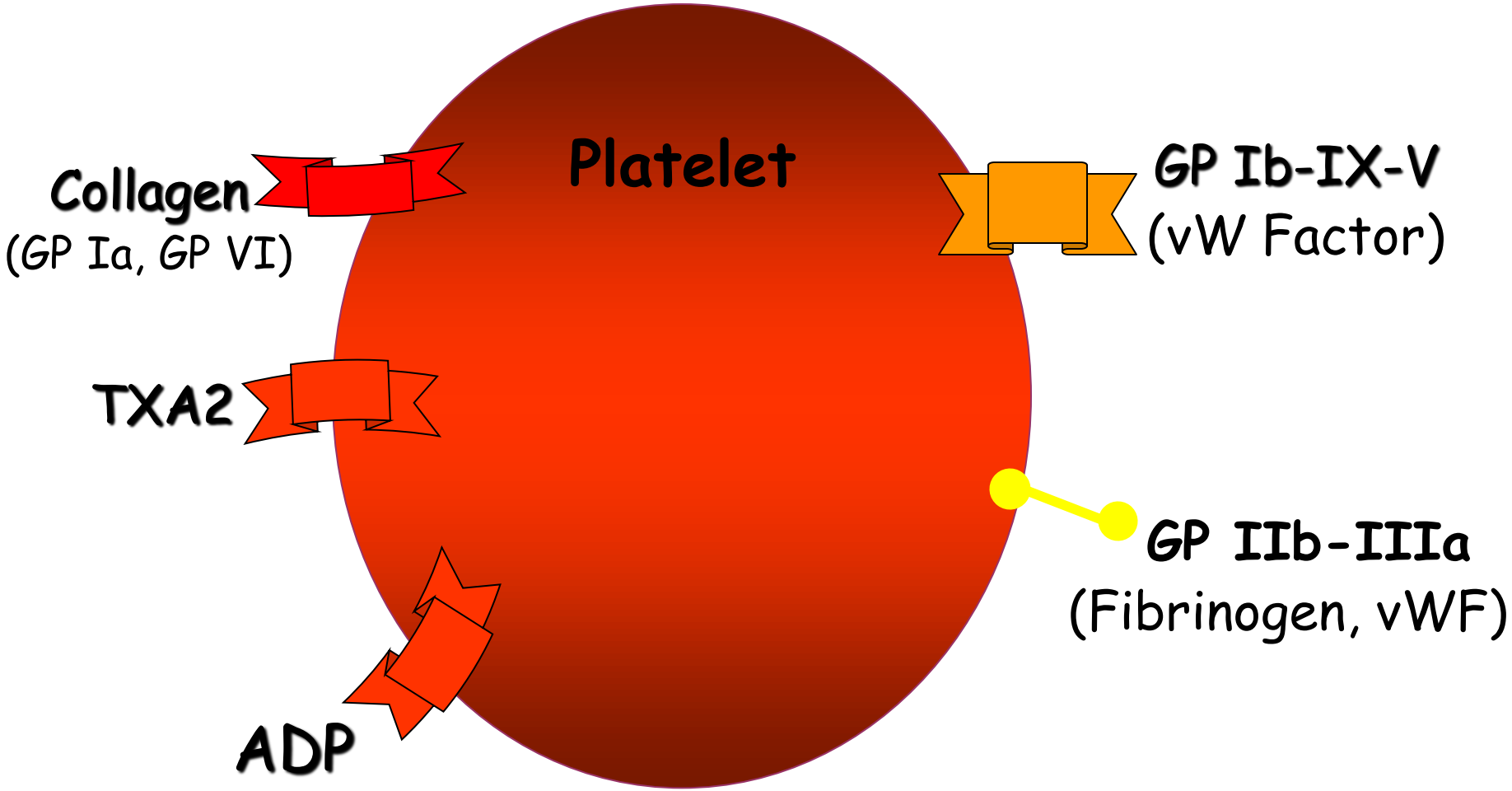
. Paris-Trousseau/Jacobsen

Adapted from Balduini et al, Haematologica 88[5]: 582-592, May 2003

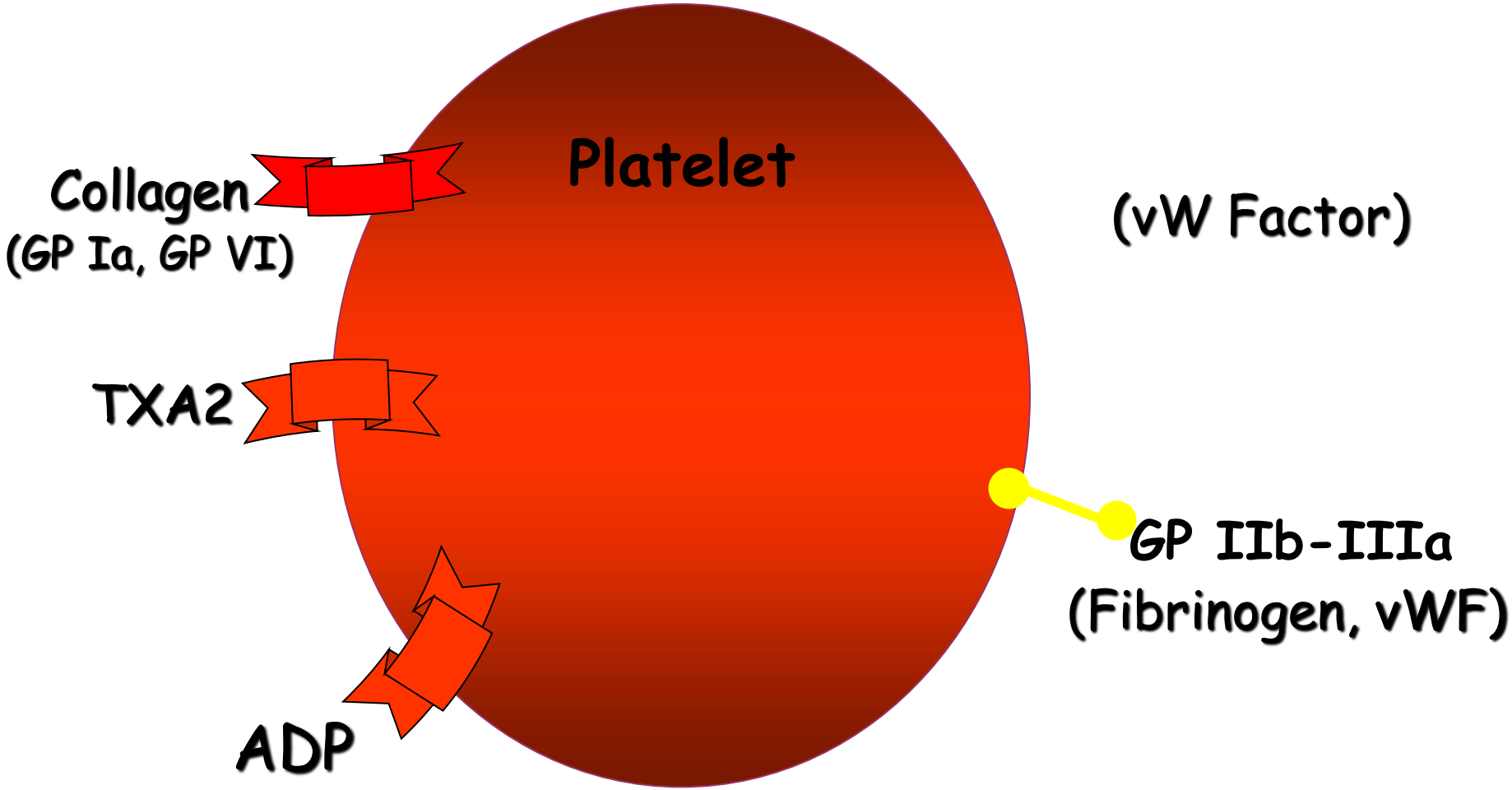
Platelet Activation

- Adhesion:
- Shape change
- Aggregation
- Release
- Clot Retraction

Bernard-Soulier Syndrome



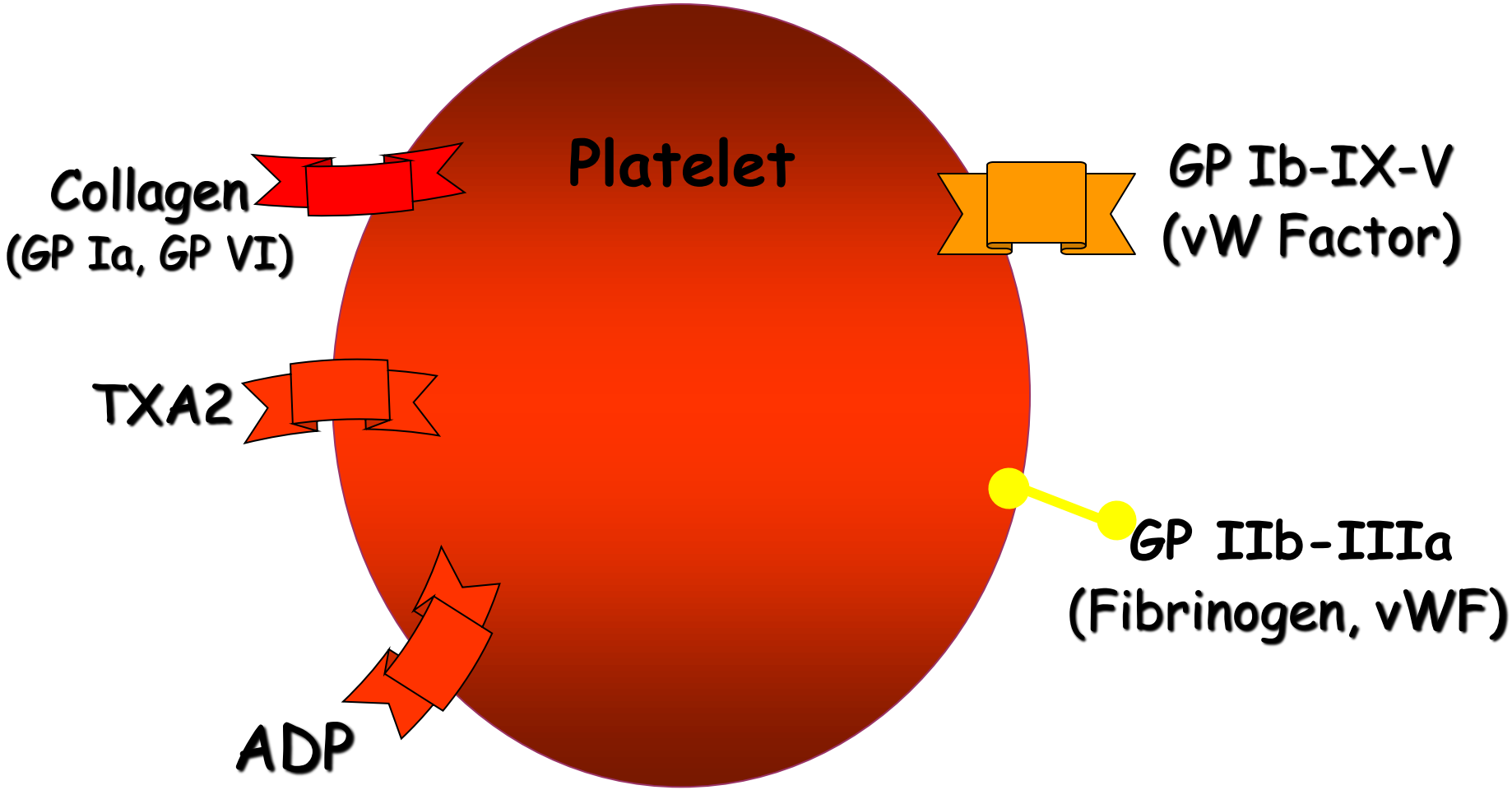
Bernard-Soulier Syndrome



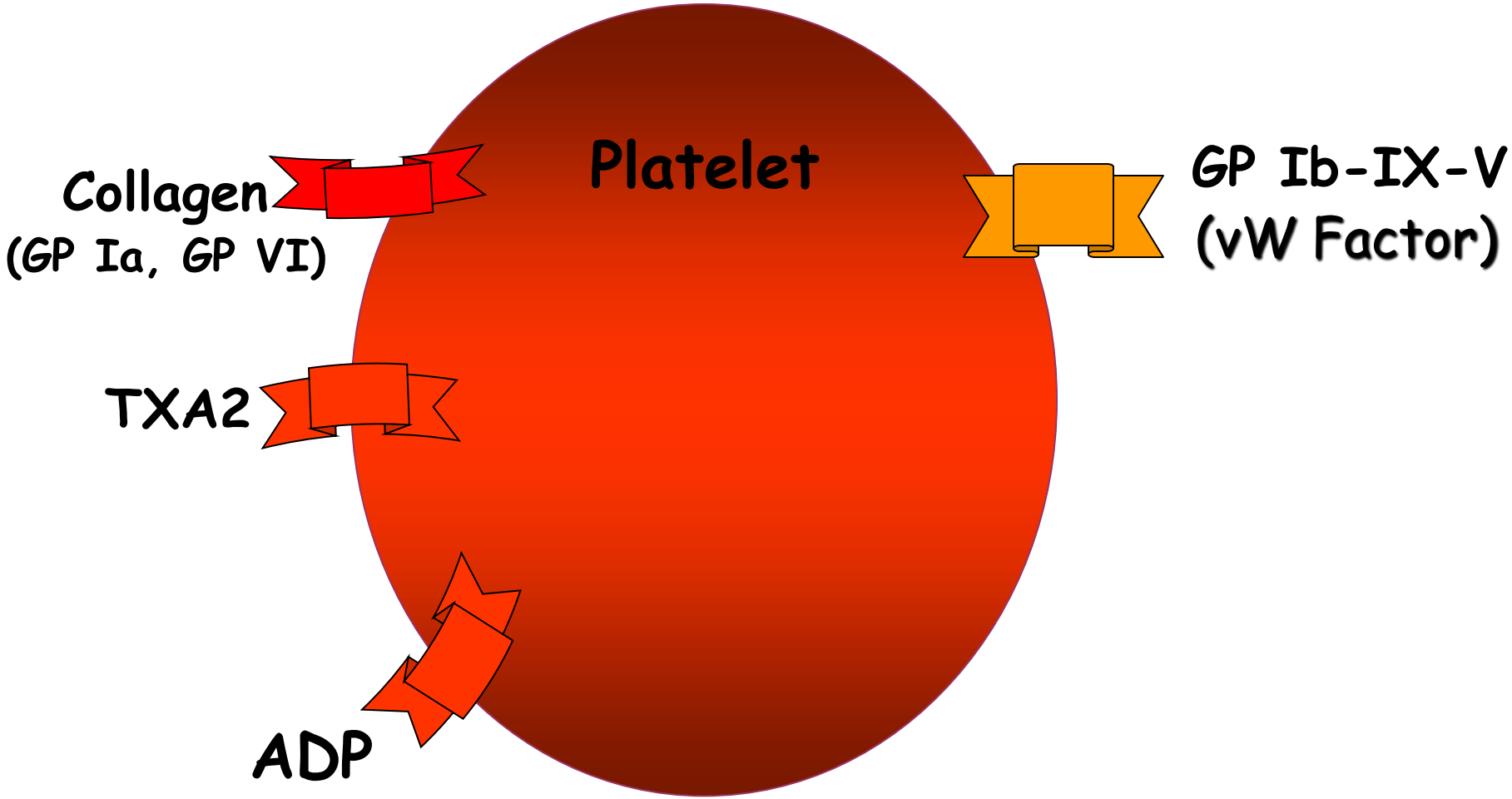
Platelet Activation

- **Adhesion:** Bernard-Soulier Syndrome (BSS)
- Shape change
- Aggregation
- Release
- Clot Retraction

Glanzmann Thromasthenia



Glanzmann Thromasthenia



Platelet Activation

- Adhesion:
- Shape change
- Aggregation Glanzmann Thrombashenia
- Release
- Clot Retraction

How to investigate for a platelet disorder?

Laboratory Testing of Platelet Functions

- Platelet count (& shape)
- Electron-microscopy
- Bleeding time
- Platelet Aggregation
- Platelet Function Analyzer (PFA-100)
- Flow-cytometry
- Granule release products

Bleeding Time

platelet function test

Platelet Aggregometry

Laboratory Testing of Platelet Functions

Platelet Aggregation

in (PRP) Platelet rich plasma):

Provides information on time course of plat. activation.

Agonists:

ADP

Adrenaline

Collagen

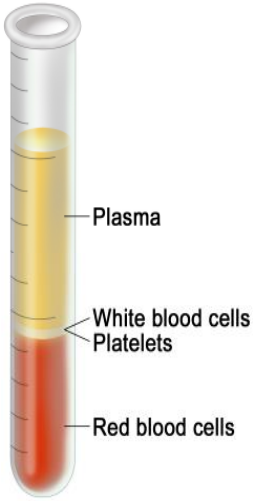
Arachidonic acid

Ristocetin

Thrombin

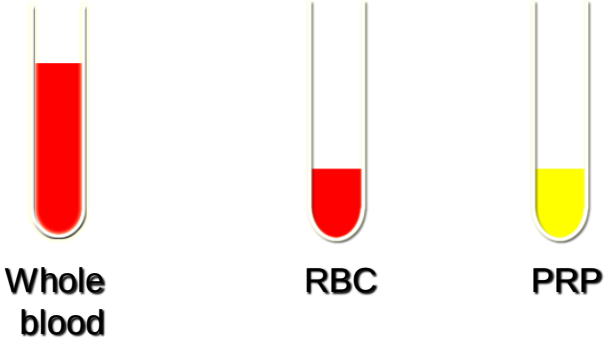
Reference ranges need to be determined for each agonist

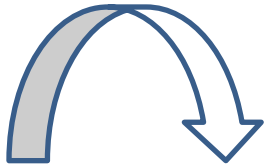
Platelet Aggregation

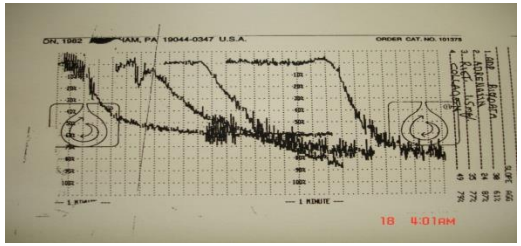


Agonists:

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







18 4:04AM

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summary

-platelets are cell fragments derived from megakaryocyte in the bone marrow.

-Platelets play a pivotal role in haemostasis by arresting bleeding from an injured blood vessels

Bleeding can result from: Platelet defects acquired or congenital


THANK YOU