

بِسْمِ اللّٰهِ الرَّحْمٰنِ الرَّحِیْمِ



Hemostasis

Dr. Abeer Al-Ghumlas

Objectives

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

- 1. Recognize different stages of hemostasis**
- 2. Describe formation and development of platelet**
- 3. Describe the role of platelets in hemostasis.**
- 4. Recognize different clotting factors**
- 5. Describe the cascade of clotting .**

6. Describe the cascade of intrinsic pathway.
5. Describe the cascade of extrinsic and common pathways.
6. Recognize the role of thrombin in coagulation
7. Recognize process of fibrinolysis and function of plasmin

Hemostasis:

**the spontaneous arrest
of bleeding from
ruptured blood vessels**

Mechanisms:

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

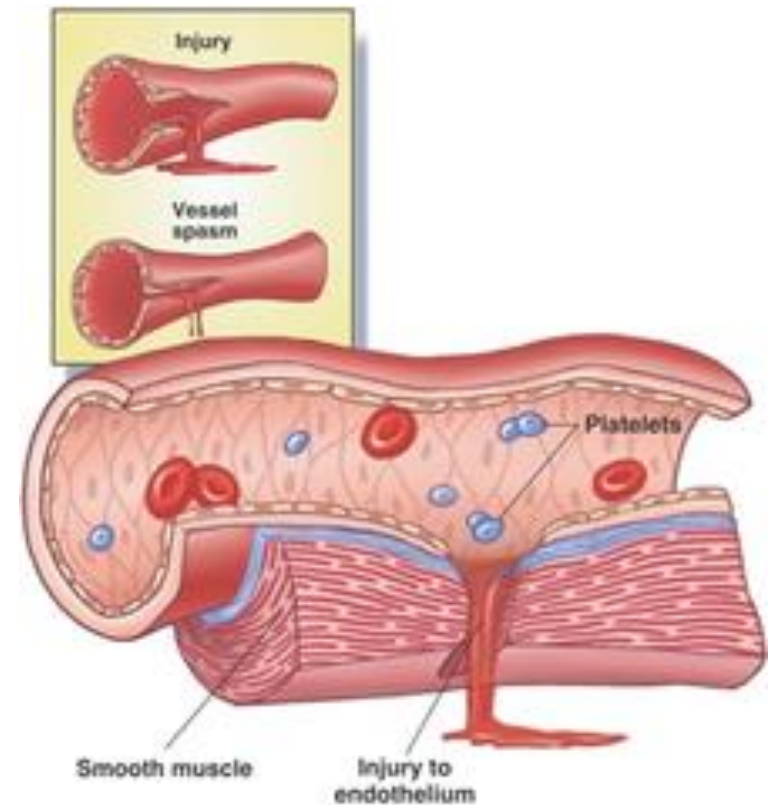
Hemostatic Mechanisms- cont

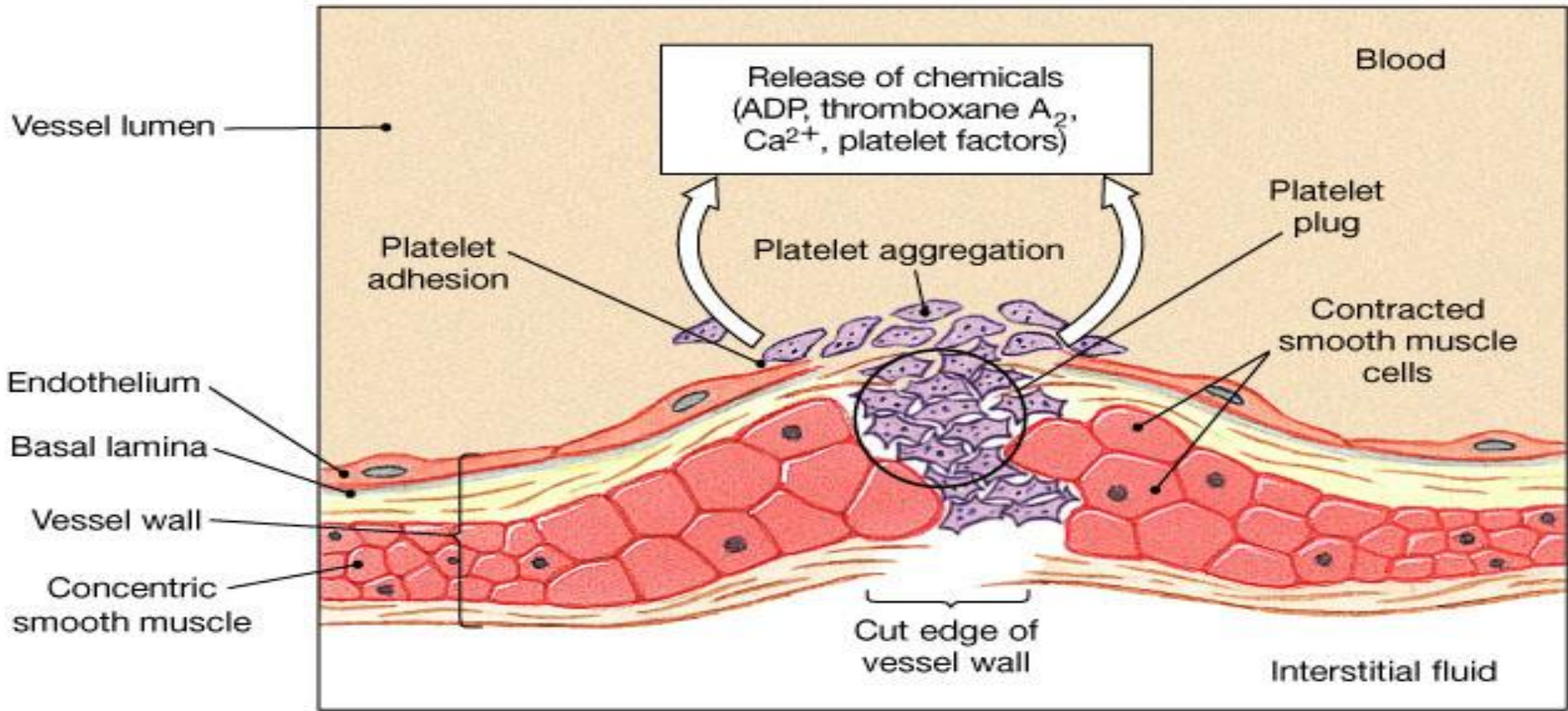
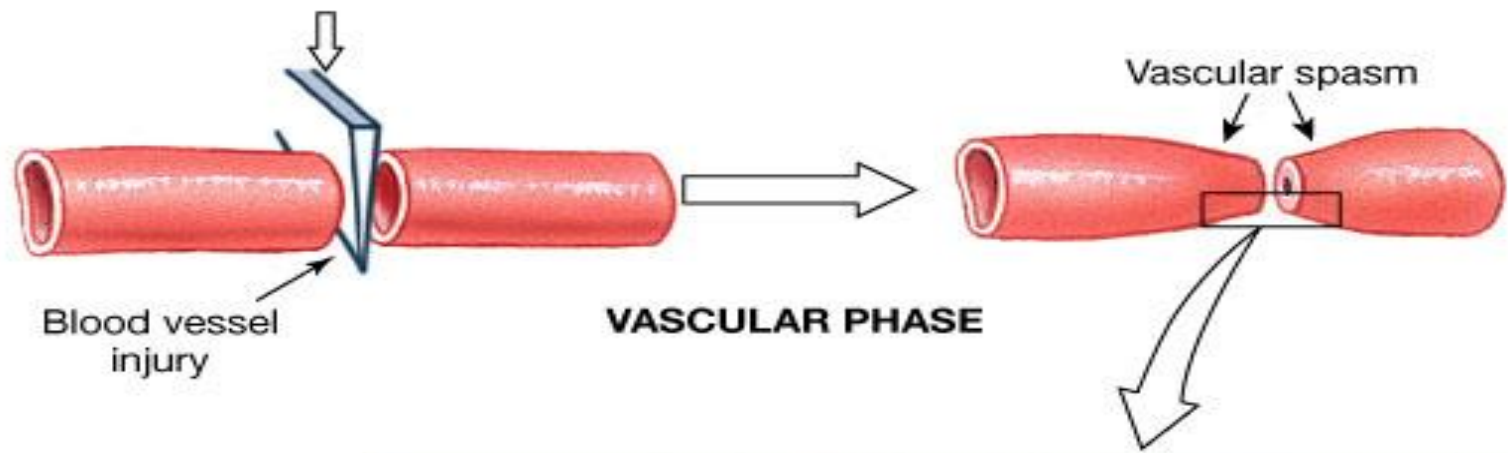
1. Vessel wall

- Immediately After injury a localized

Vasoconstriction

- Mechanism:
 - Systemic release of adrenaline
 - Nervous factors
 - local release of thromboxane A₂ & 5HT by platelets





PLATELET PHASE

Hemostatic Mechanisms:

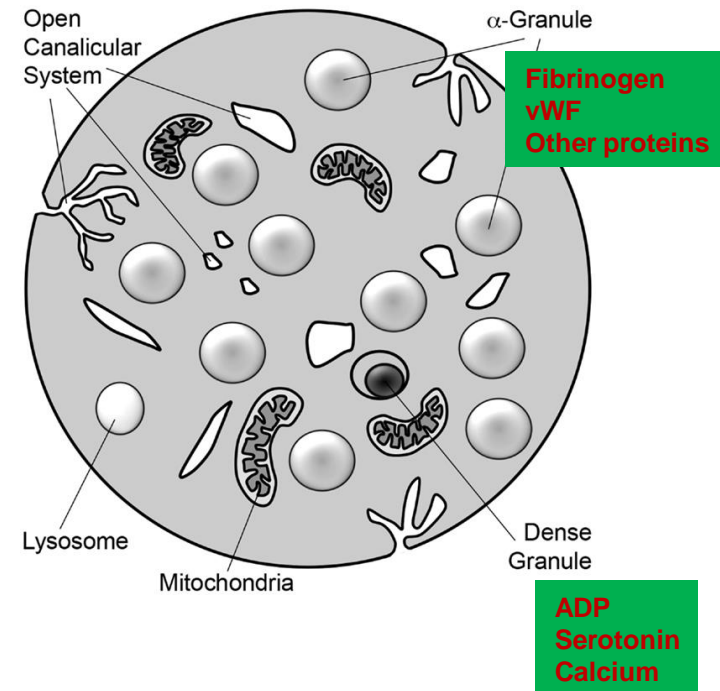
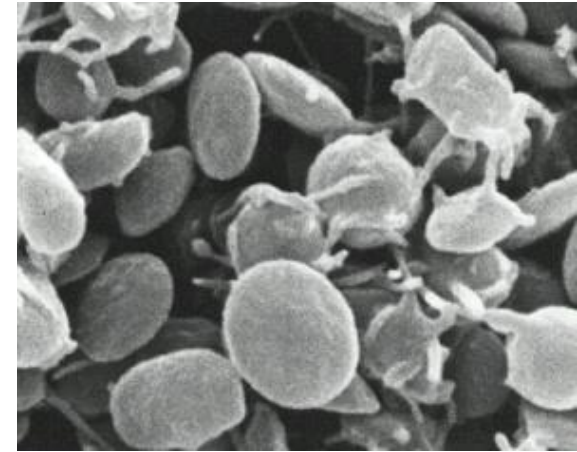
- Mechanisms:
 - Vessel wall
 - Platelet
 - Blood coagulation
 - Fibrinolytic system

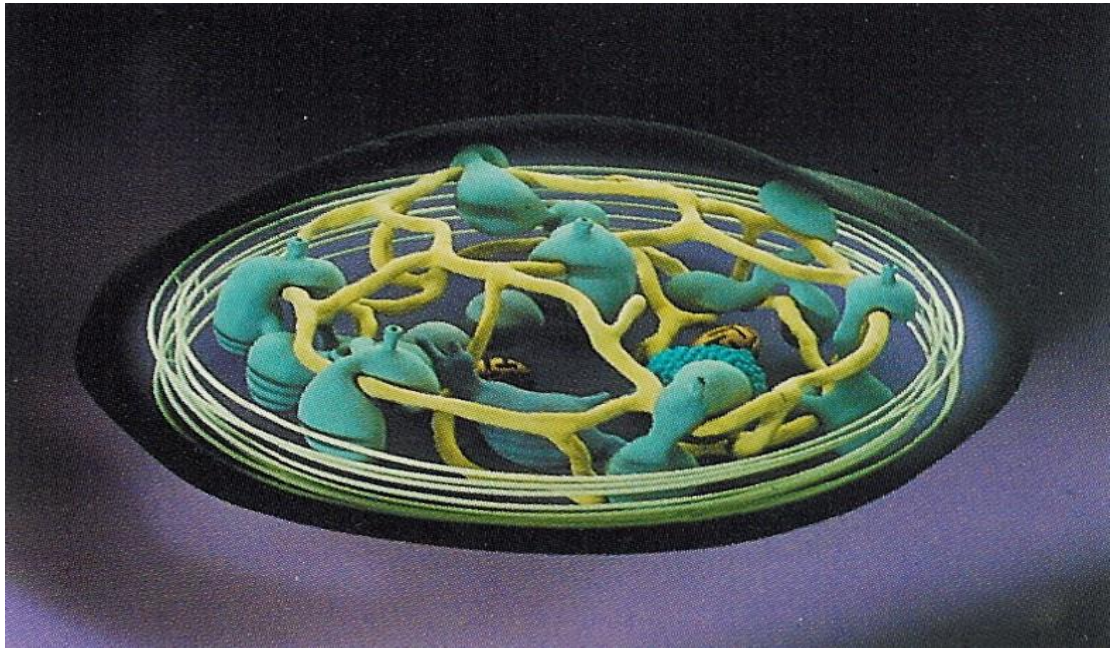
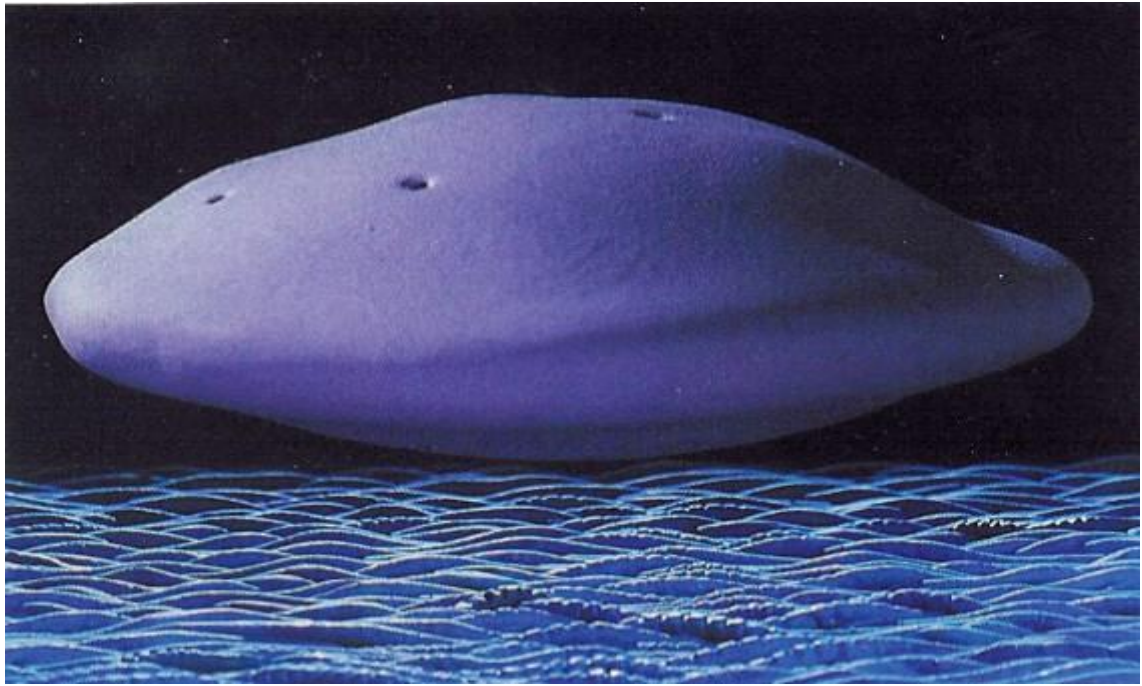
platelets

- Thrombocytes
- are Fragments of megakaryocytes in the bone marrow
- Regulation of thrombopoiesis
By:
Thrombopoietin

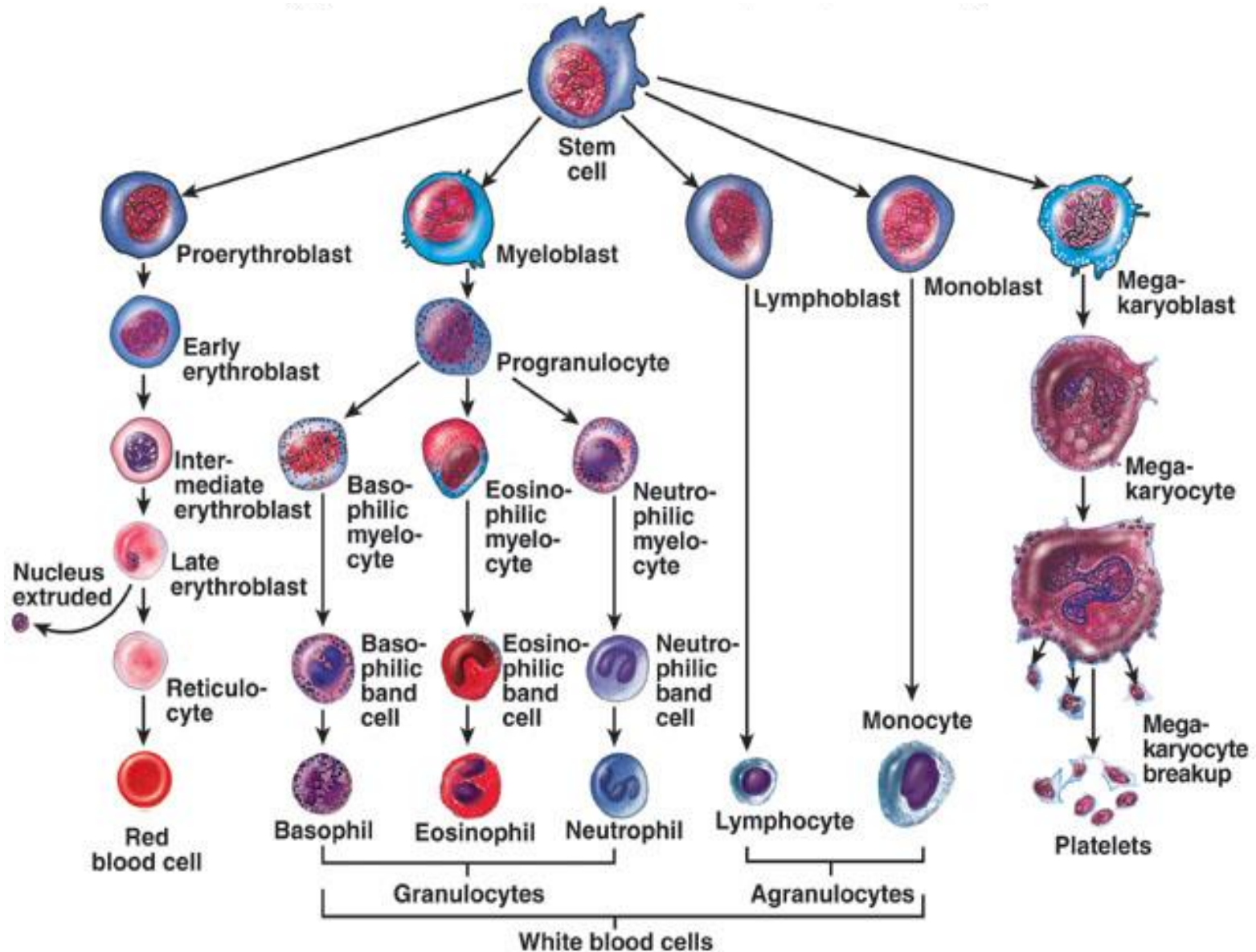
Platelets

- small disc shaped cells
- Platelet count = $150 \times 10^3 - 300 \times 10^3 / \text{ml}$,
- life span 8-12 days
- Contain high calcium content & rich in ADP
- Active cells contain contractile protein.





Hematopoiesis

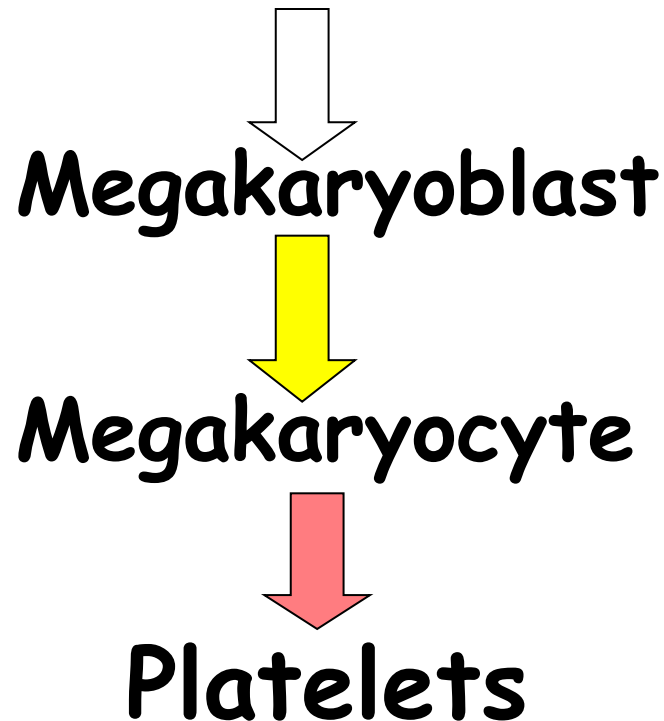


Platelets - cont.

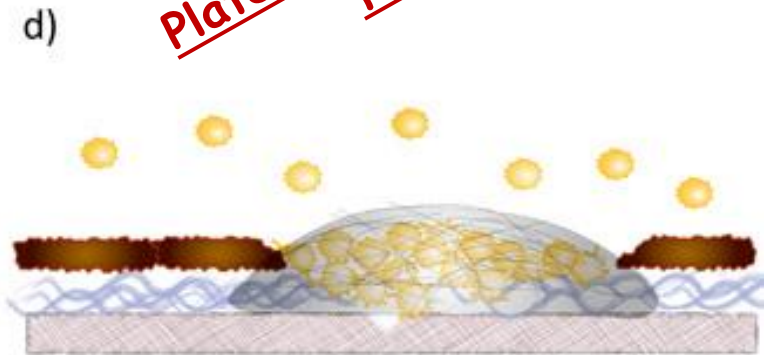
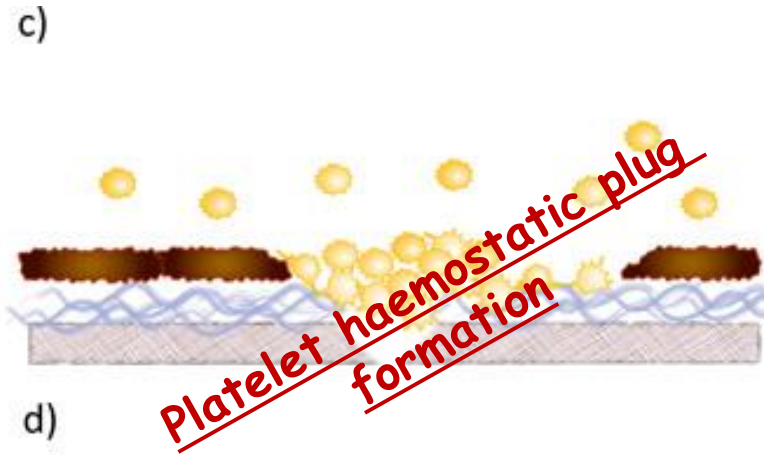
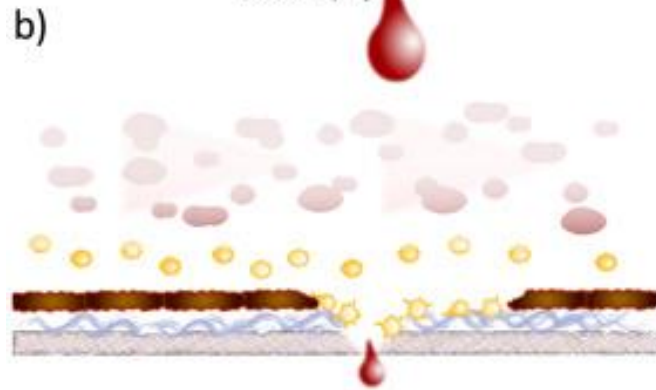
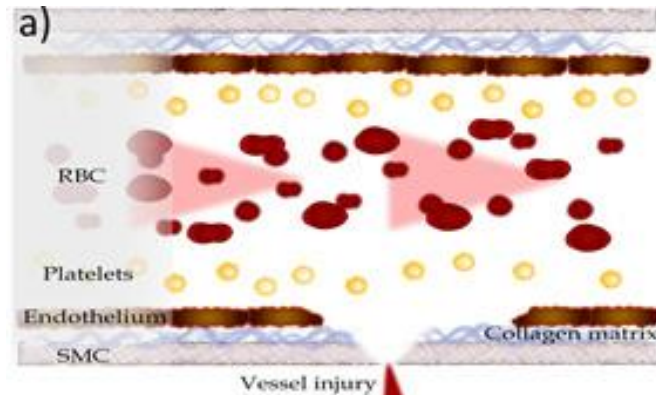
Site of formation:

Bone marrow

Steps: Stem cell



Platelet haemostatic plug formation

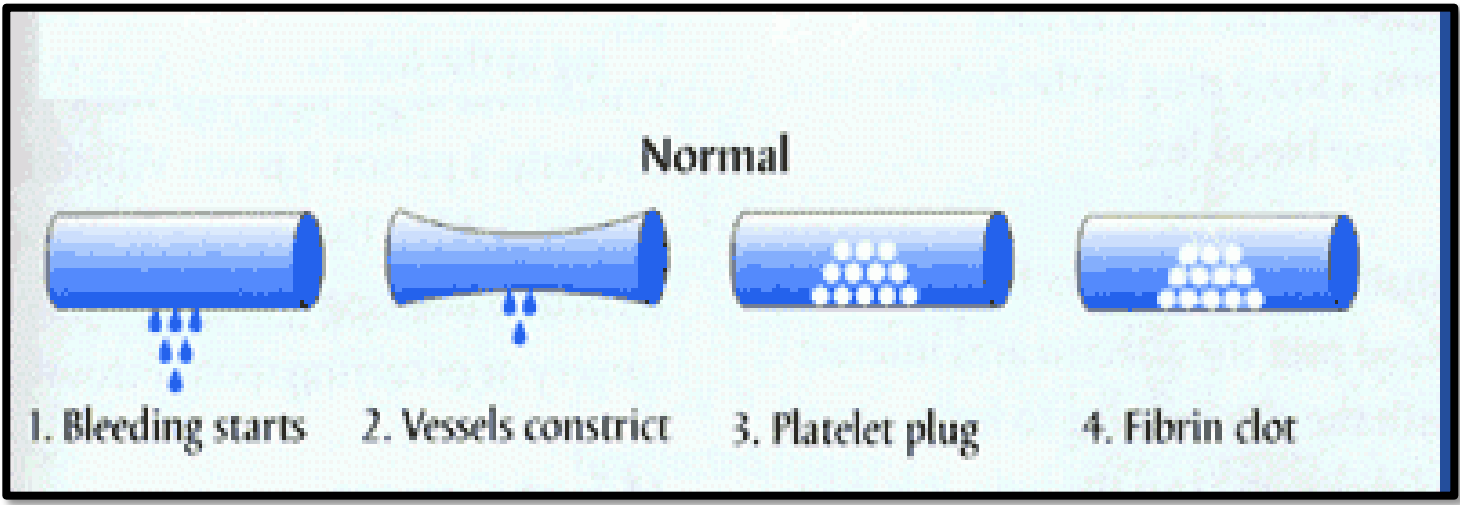


Platelet Functions

Begins with Platelet activation

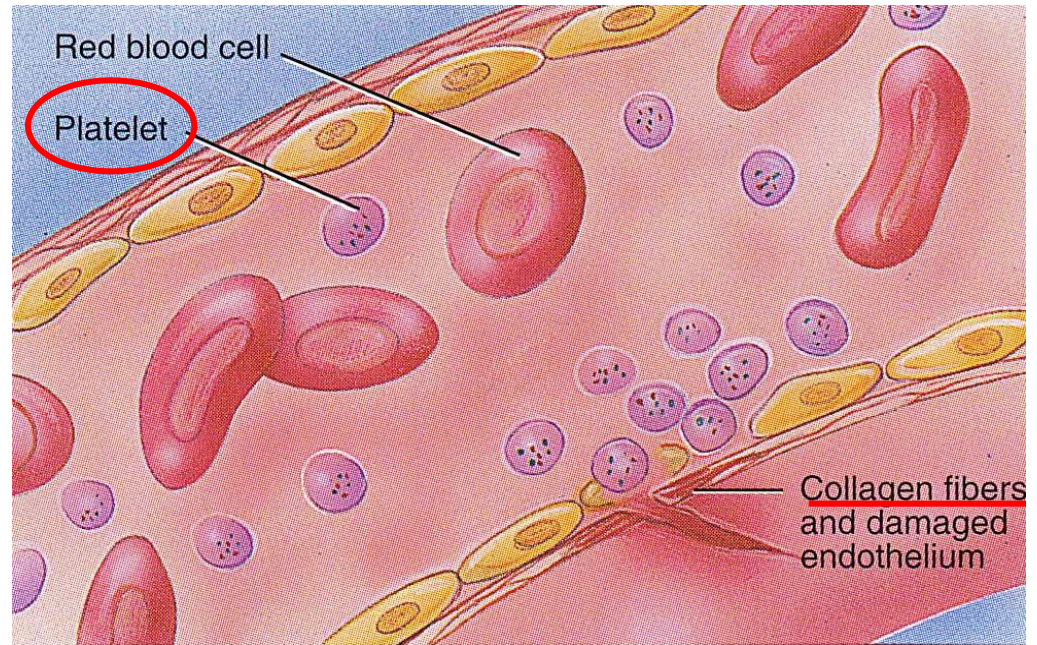
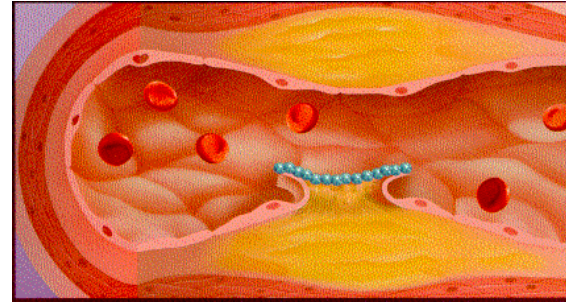
Platelet Activation

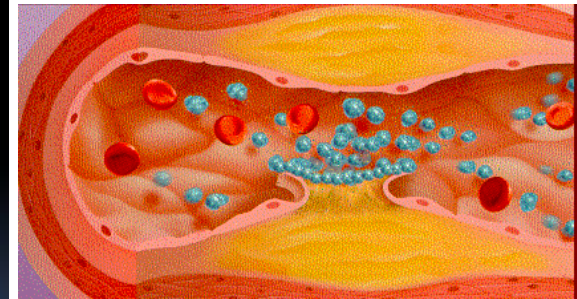
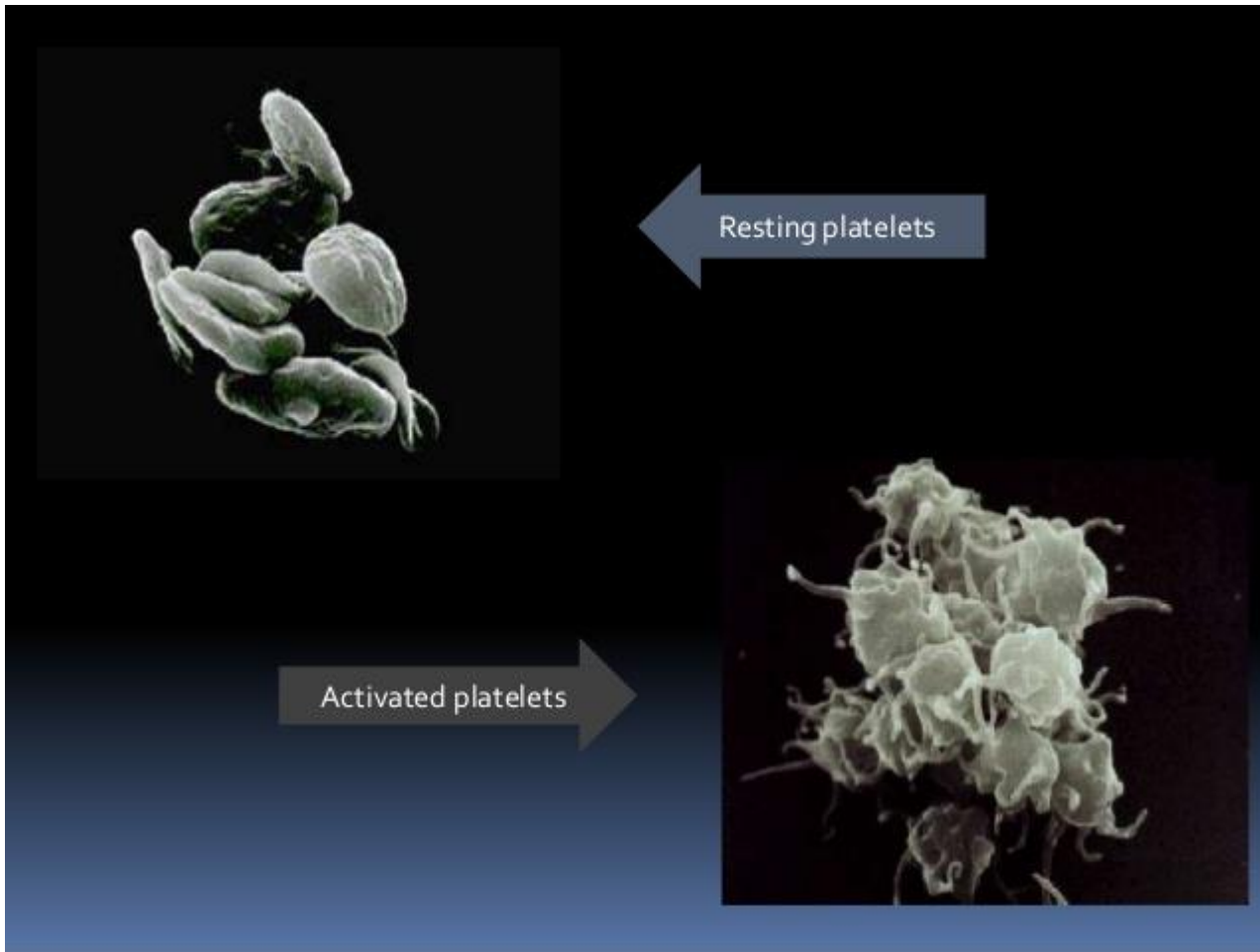
- **Adhesion**
- **Shape change**
- **Aggregation**
- **Release**
- **Clot Retraction**



Platelet Adhesion

- Exposed collagen attracts platelets
- Platelets stick to exposed collagen underlying damaged endothelial cells in vessel wall

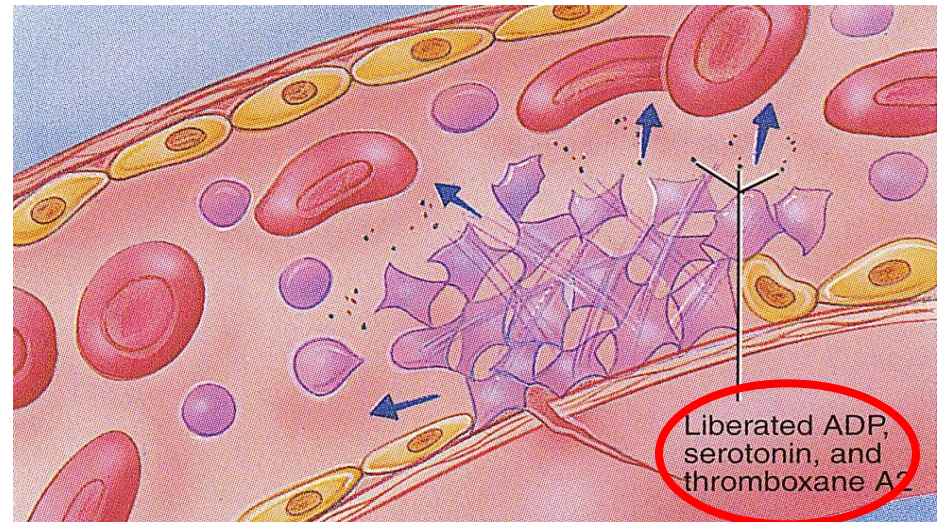
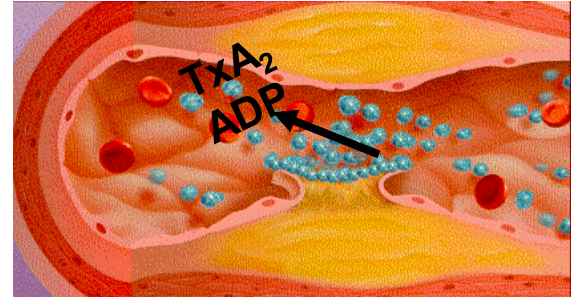




- **Platelets activated by adhesion**
- **Extend projections to make contact with each other**

Platelet Release Reaction

- Activated platelets release Serotonin, ADP & Thromboxane A₂
- Serotonin & thromboxane A₂ are vasoconstrictors decreasing blood flow through the injured vessel.
- ADP & Thromboxane A₂ (TXA₂) → ↑ the stickiness of platelets → ↑ Platelets aggregation → plugging of the cut vessel



Activated Platelets

Secrete:

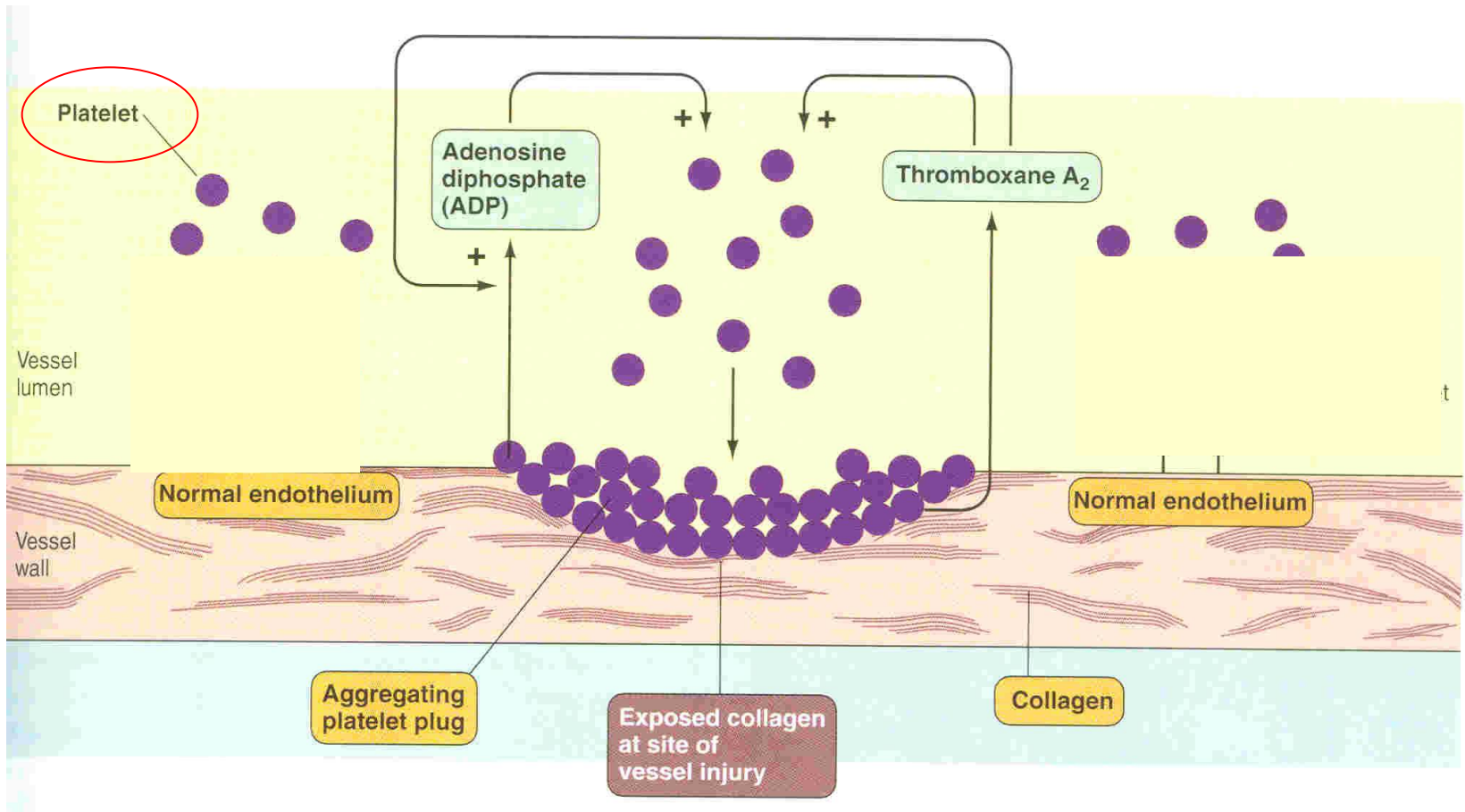
1. 5HT → vasoconstriction
2. ADP
3. Platelet phospholipid (PF3) → clot formation
4. Thromboxane A2 (TXA2) is a prostaglandin formed from arachidonic acid

Function:

- vasoconstriction
- Platelet aggregation

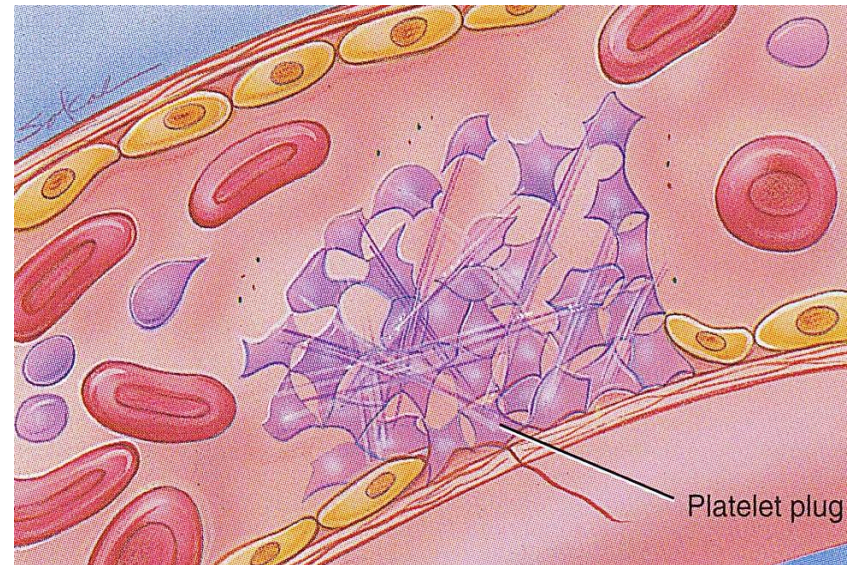
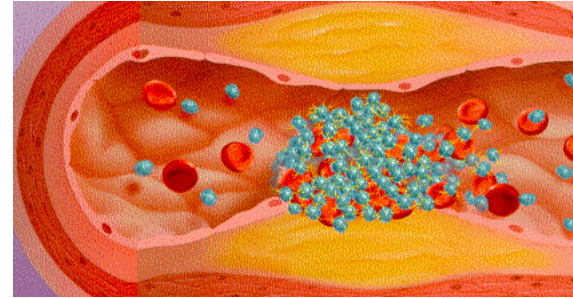
(TXA2 inhibited by aspirin)

Platelets aggregation

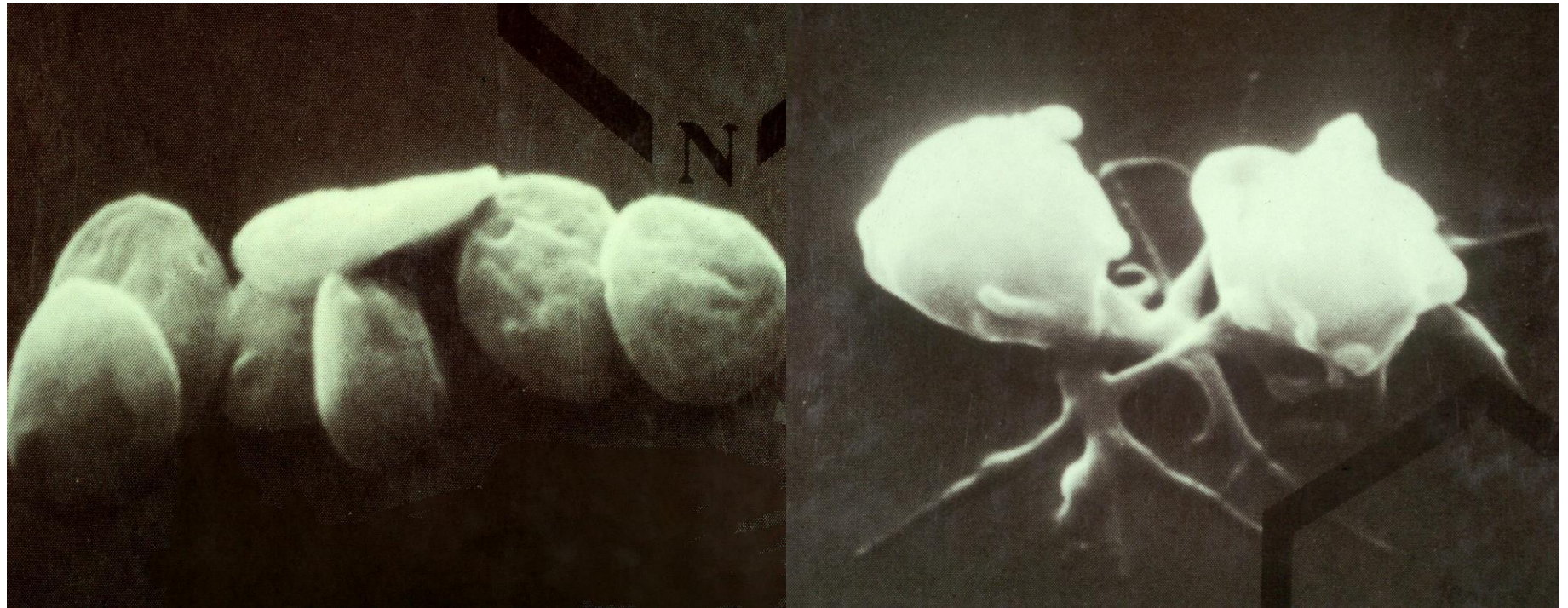


Platelet Aggregation

- Activated platelets stick together and activate new platelets to form a mass called a platelet plug
- Plug reinforced by fibrin threads formed during clotting process



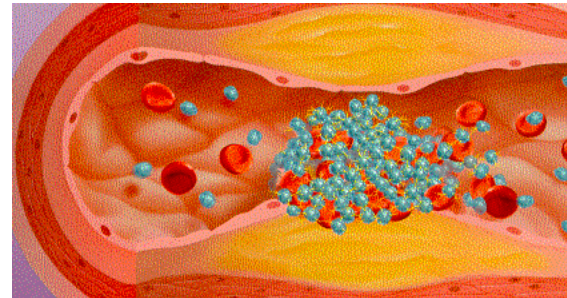
Platelet shape change and Aggregation

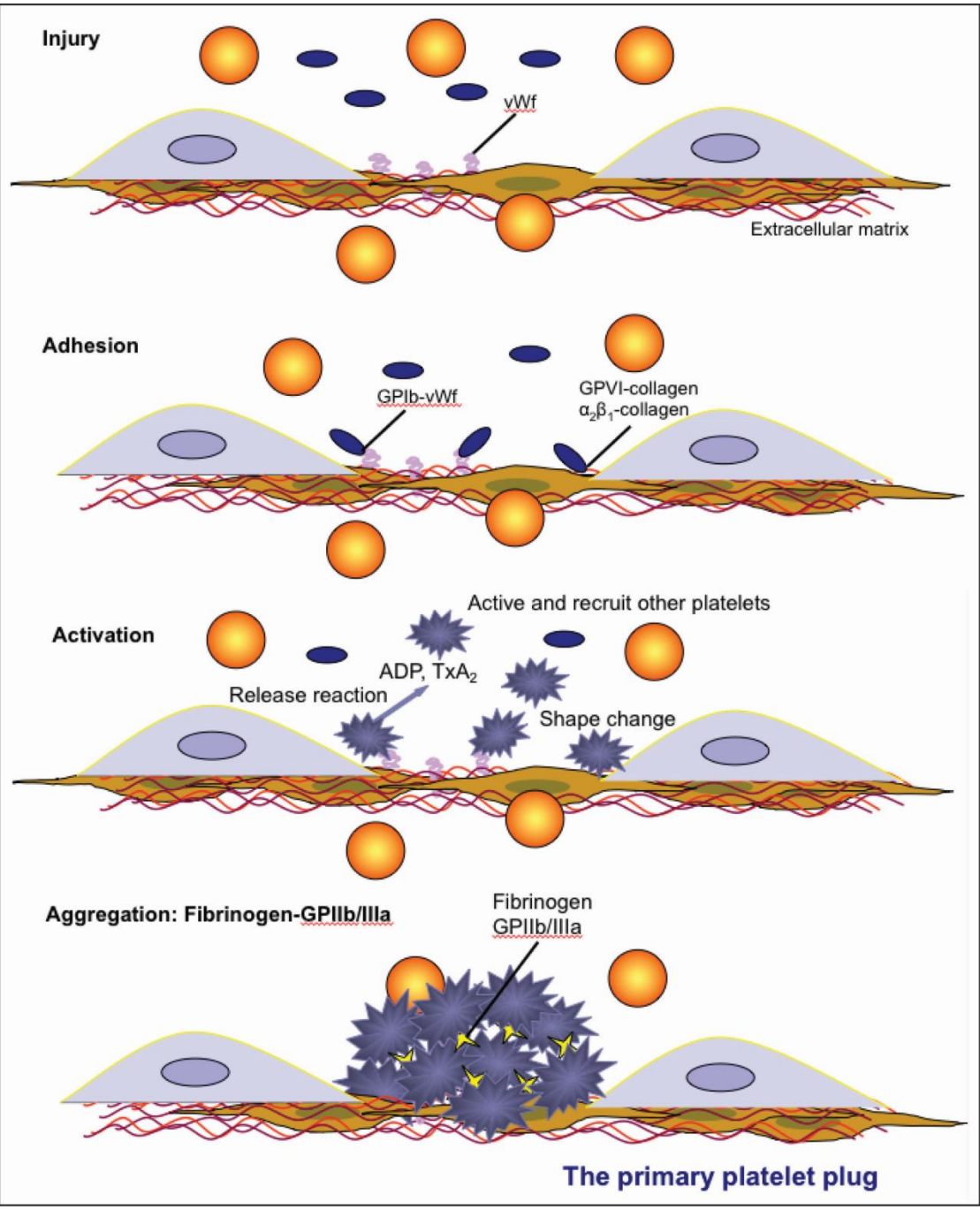


Platelet Activation

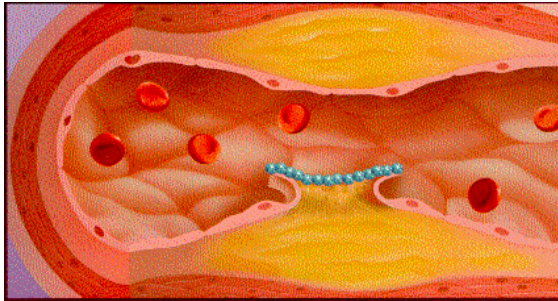
- Clot Retraction:

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

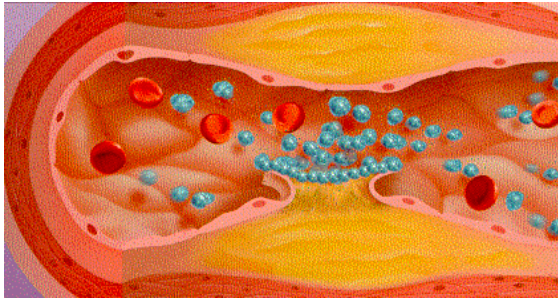




Platelet function

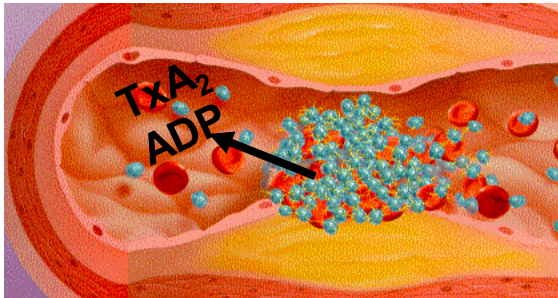


Adhesion

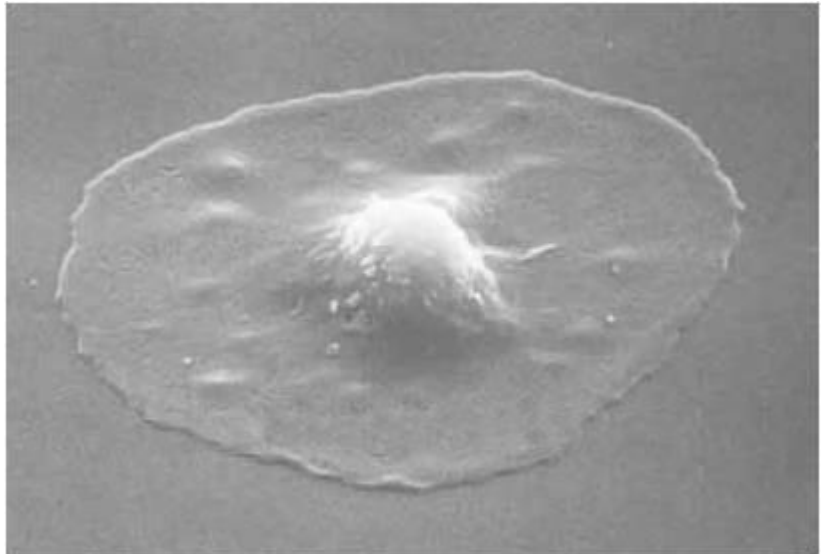
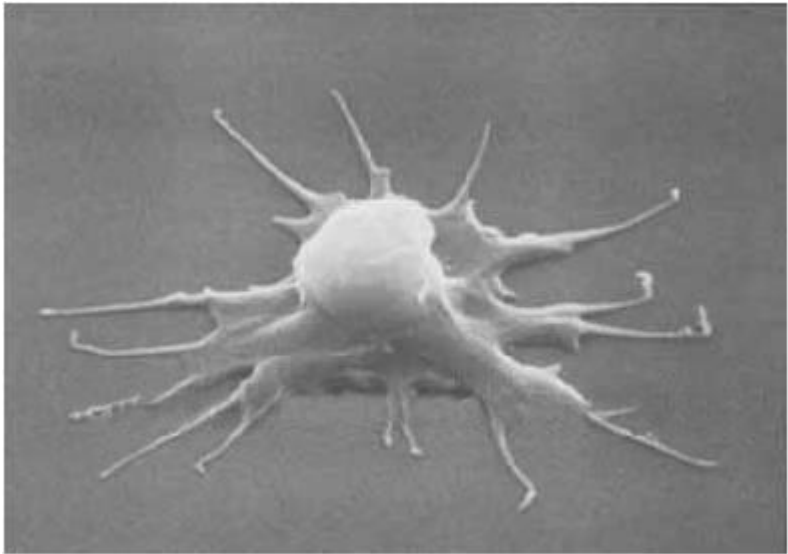
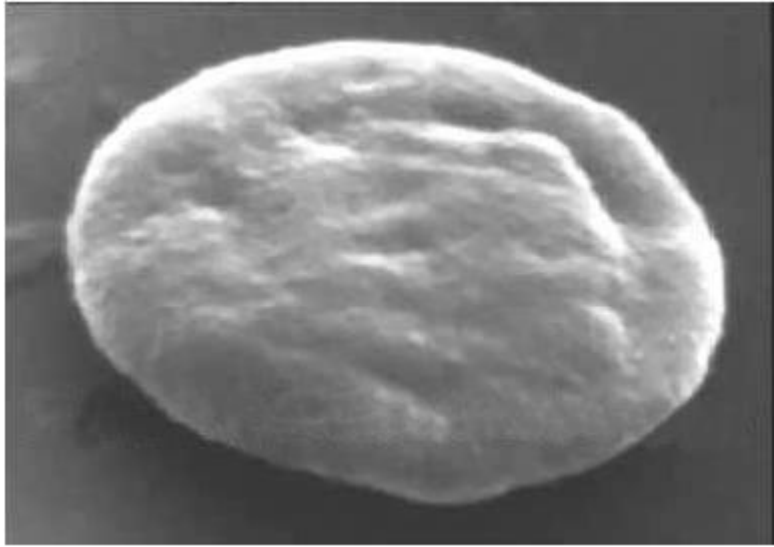


Activation

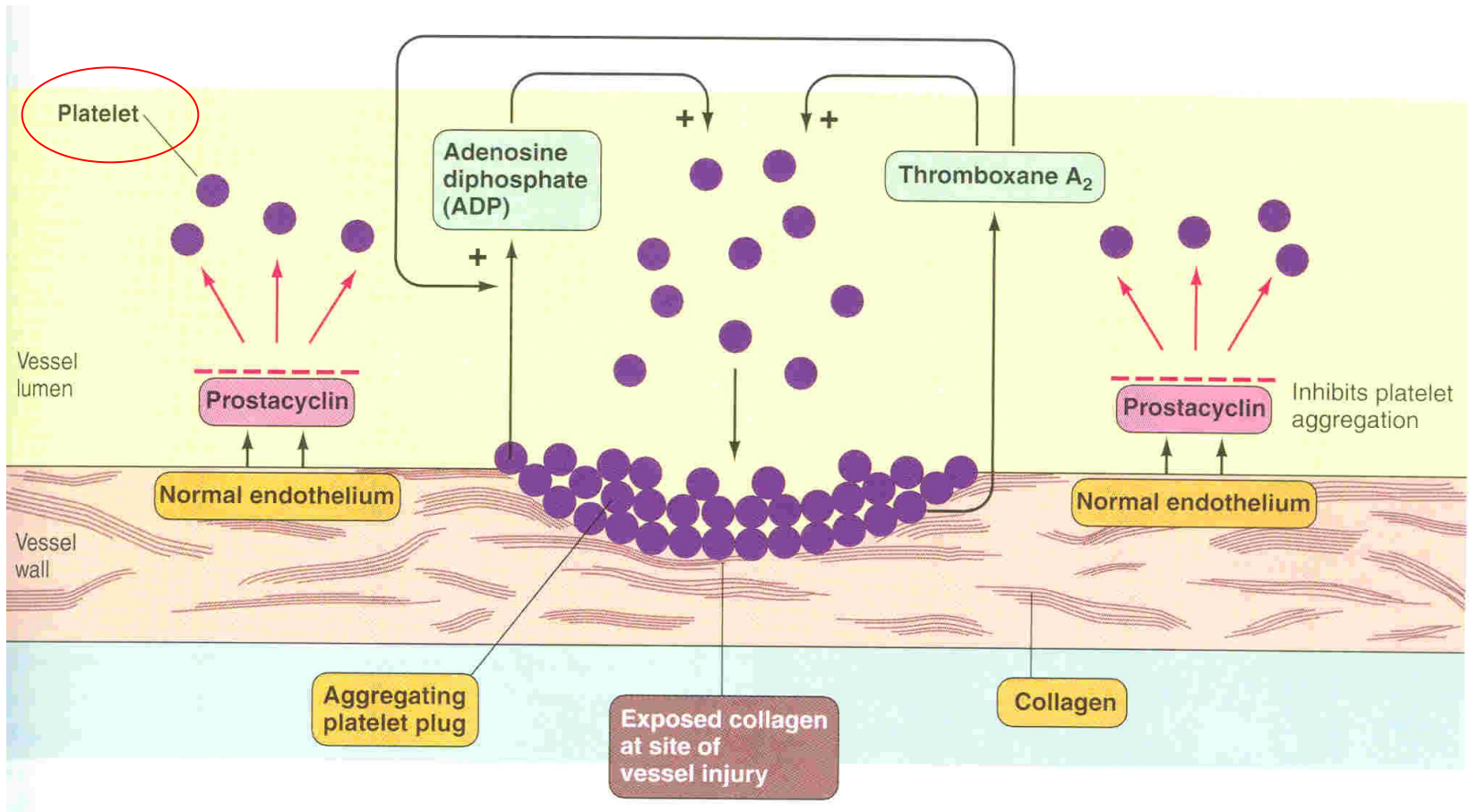
Aggregation



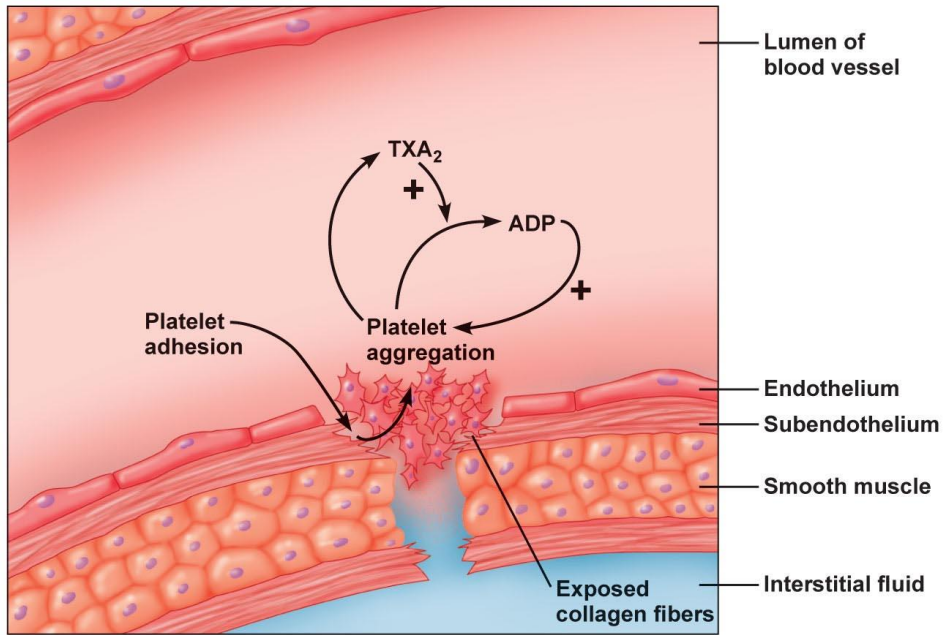
Secretion



Platelets aggregation

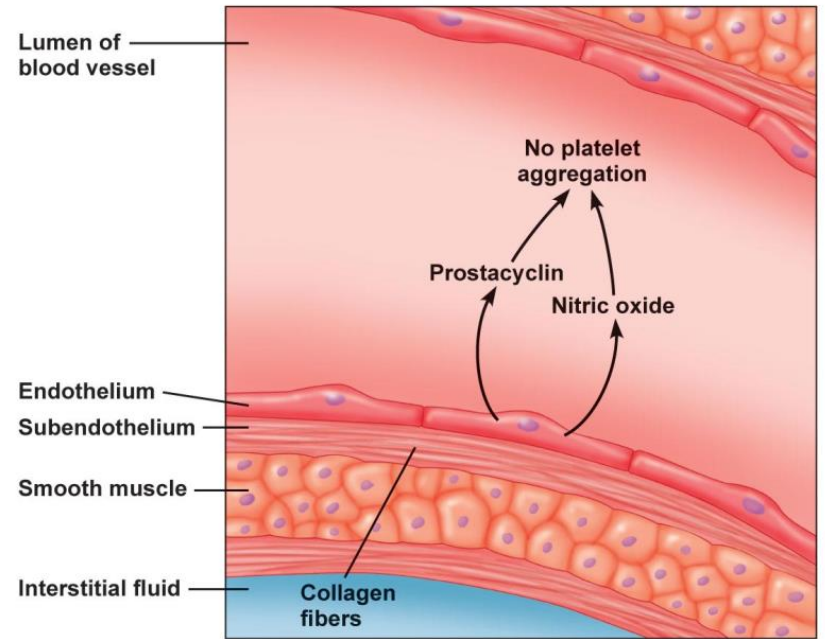


- Intact endothelium secret prostacyclin and NO which inhibit aggregation



(a) Damaged blood vessel endothelium

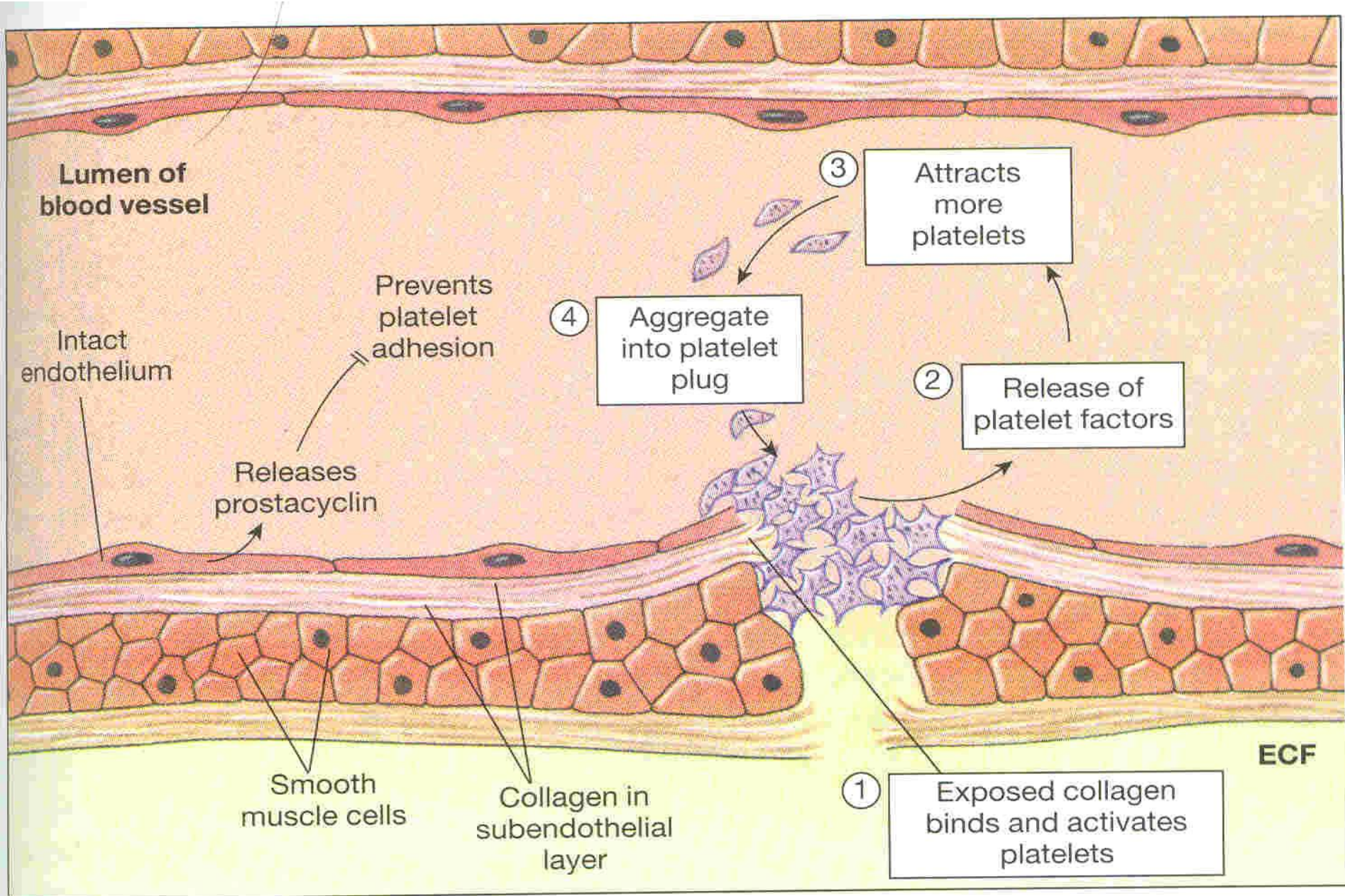
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(b) Normal blood vessel endothelium

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Platelet plug formation



Memostatic Mechanisms:

- **Mechanisms:**
 - **Vessel wall**
 - **Platelet**
 - **Blood coagulation**
 - **Fibrinolytic system**

Clotting Factors

Circulate in plasma in inactive state

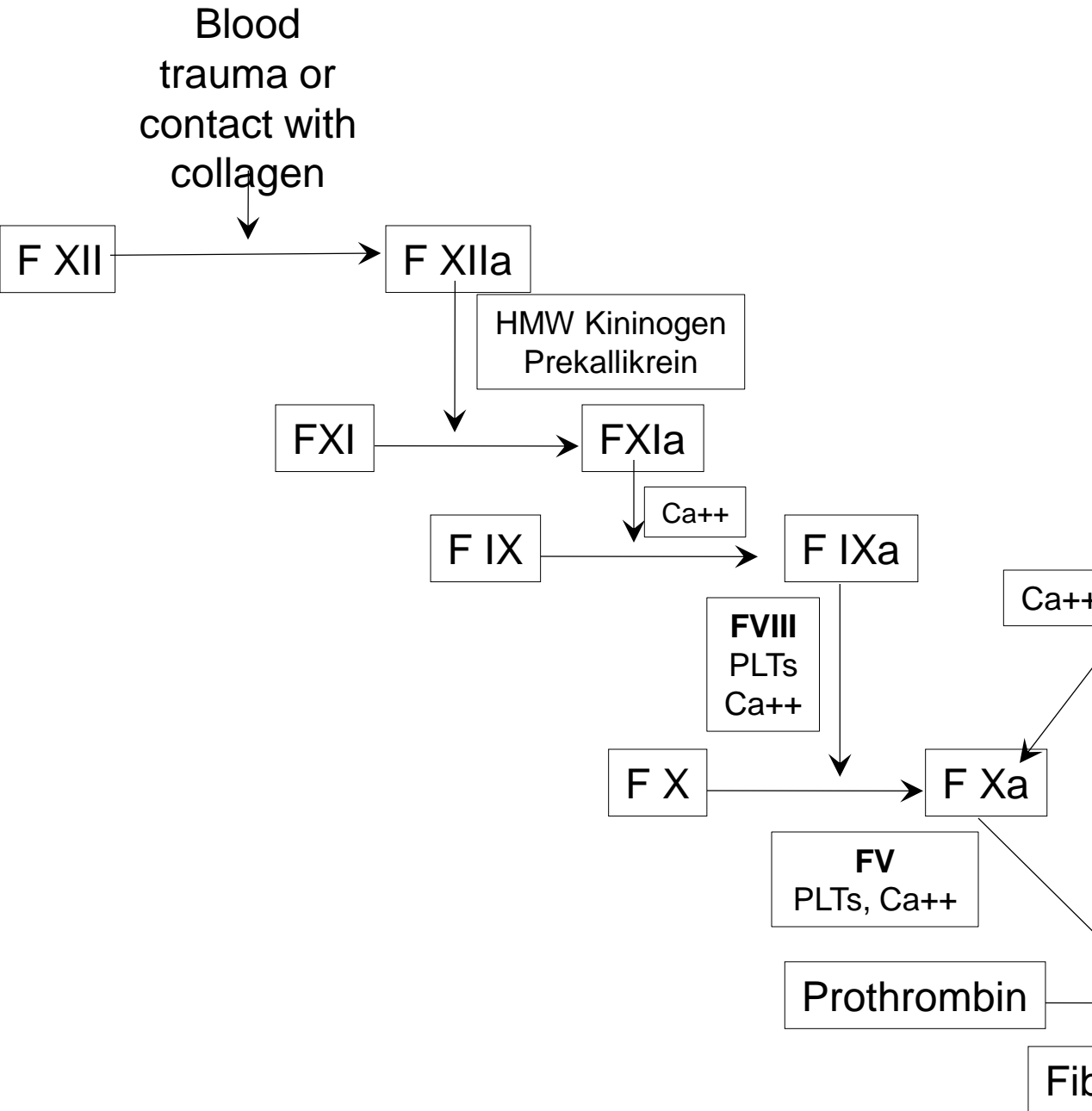
Factors	Names
I	Fibrinogen
II	Prothrombin
III	Thromboplastin
IV	Calcium
V	Labile factor
VII	Stable factor
VIII	Antihemophilic factor A
IX	Antihemophilic factor B
X	Stuart-Power factor
XI	Plasma thromboplastin antecedent (PTA)
XII	Hagman factor
XIII	Fibrin stabilizing factors

Blood coagulation

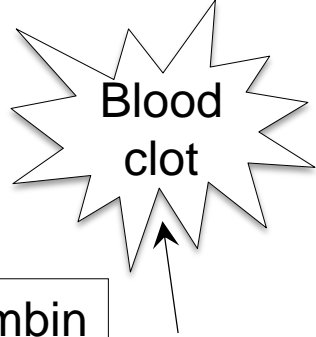
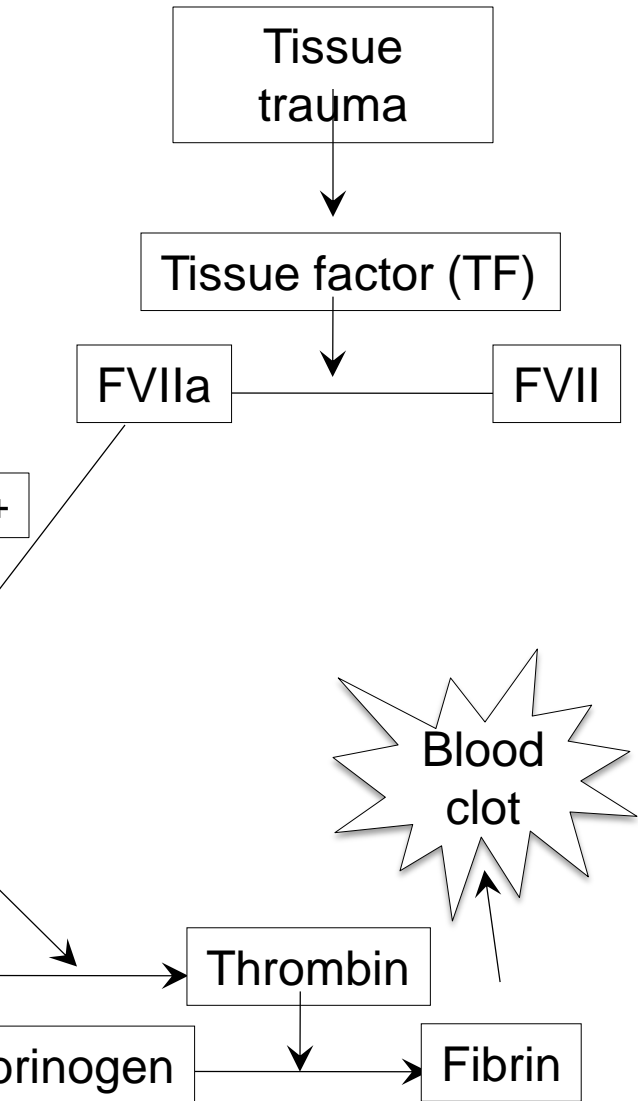
(clot formation)

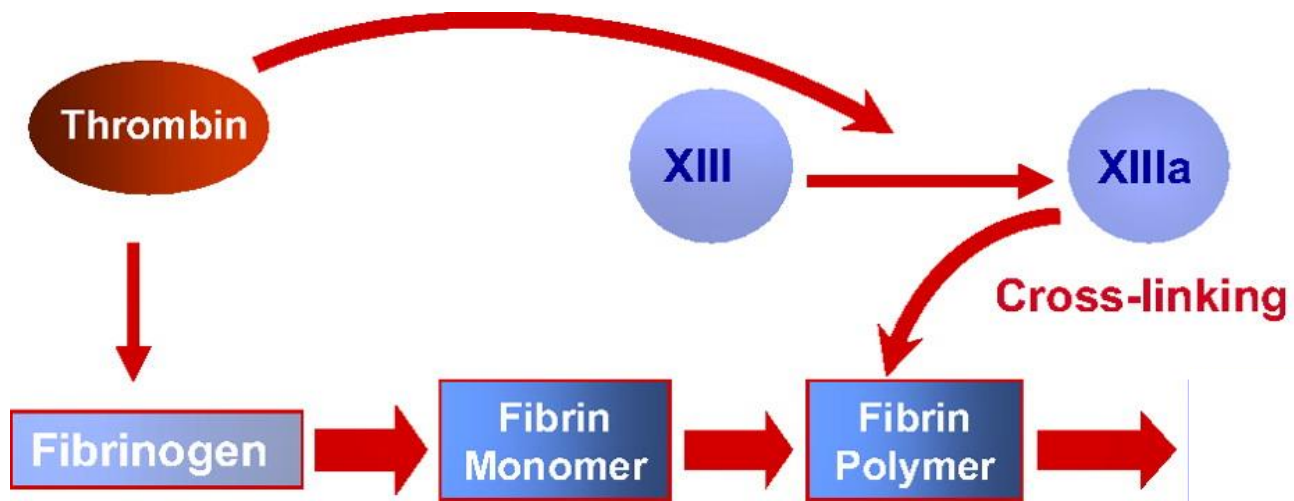
- A series of biochemical reactions leading to the formation of a blood clot
- This reaction leads to the activation of thrombin enzyme from inactive form prothrombin
- Thrombin will change fibrinogen (plasma protein) to fibrin (insoluble protein)
- Prothrombin (inactive thrombin) is activated by a long intrinsic or short extrinsic pathways

The Intrinsic Pathway



The Extrinsic Pathway

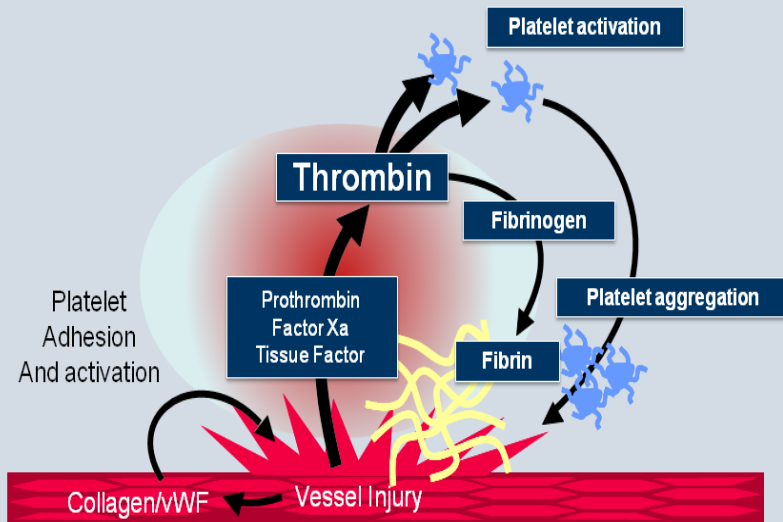




Thrombin

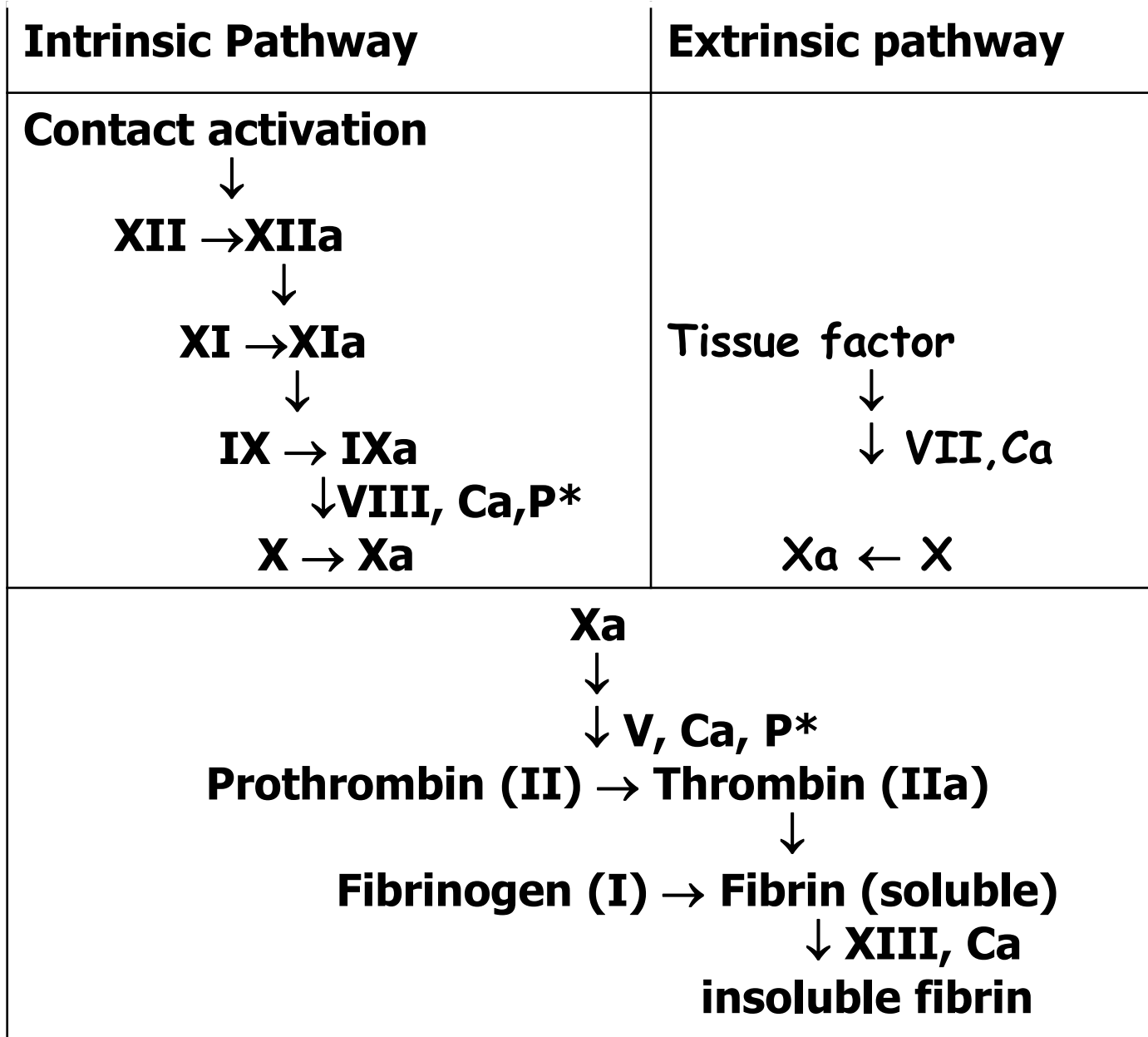
Critical Role of Thrombin

Thrombin is the link between vascular injury, coagulation, and platelet activation



Coughlin SR. *Nature*. 2000;407:258-64; Monroe DM et al. *ATVB* 2002;22:1381-9.

- Thrombin changes fibrinogen to fibrin
- Activates factor V
- Thrombin is essential in platelet morphological changes to form primary plug
- Thrombin stimulates platelets to release ADP & thromboxane A₂; both stimulate further platelets aggregation



P* = phospholipid from platelets

Intrinsic pathway

- The trigger is the activation of factor XII by contact with foreign surface, injured blood vessel, and glass.
- Activate factor (XIIa) will activate XI
- XIa will activate IX
- IXa + VIII + platelet phospholipid + Ca activate X
- Following this step the pathway is common for both

Extrinsic pathway

- Triggered by material released from damaged tissues (tissue thromboplastin)
- tissue thromboplastin + VII + Ca → activate X

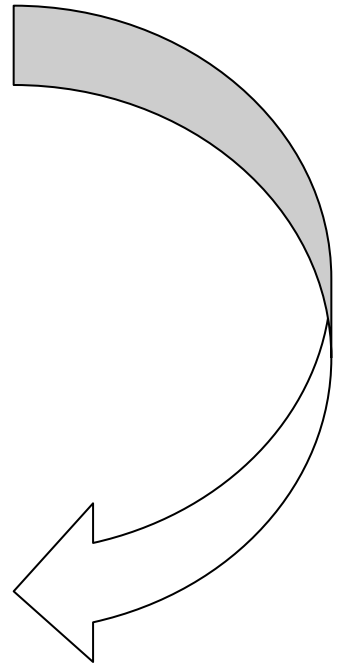
Common pathway

- Xa + V + PF3 + Ca (prothrombin activator) it is a proteolytic enzyme activate prothrombin → thrombin
- Thrombin act on fibrinogen → insoluble thread like fibrin
- Factor XIII + Ca → strong fibrin (strong clot)

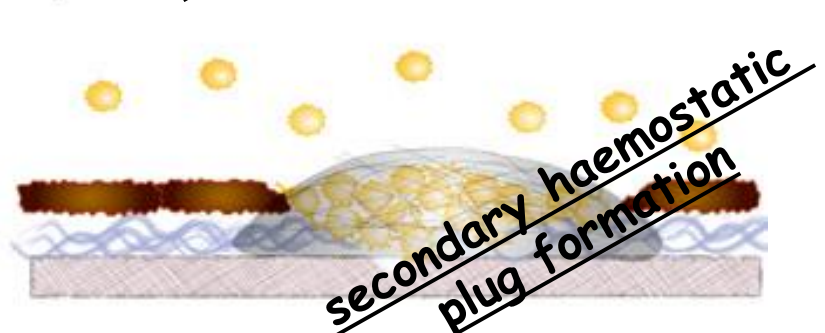
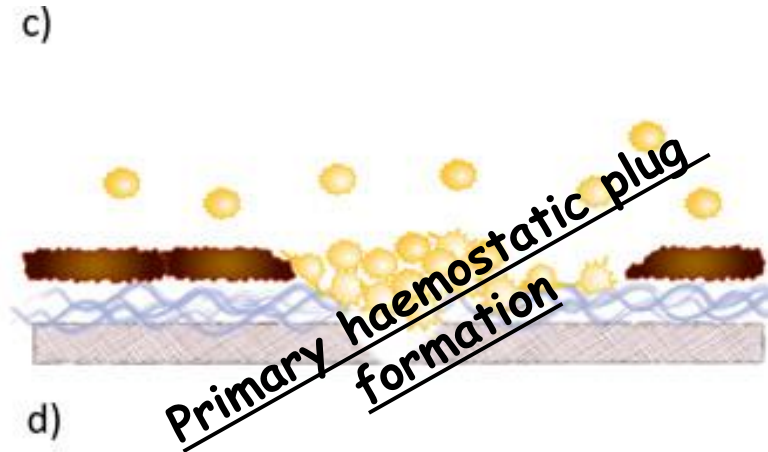
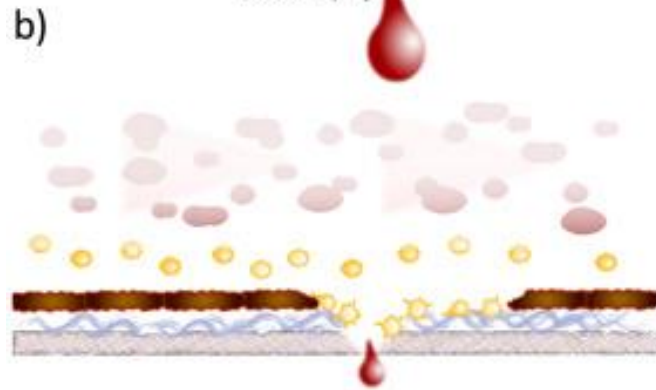
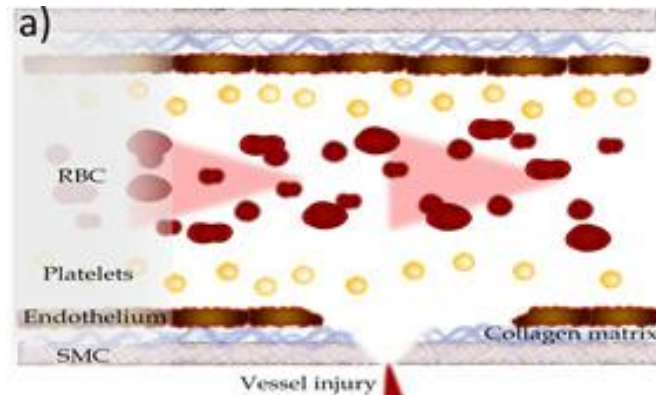
Activation Blood Coagulation

- **Intrinsic Pathway:** all clotting factors present in the blood
- **Extrinsic Pathway:** triggered by tissue factor

Common Pathway



Platelet haemostatic plug formation



Hemostasis:

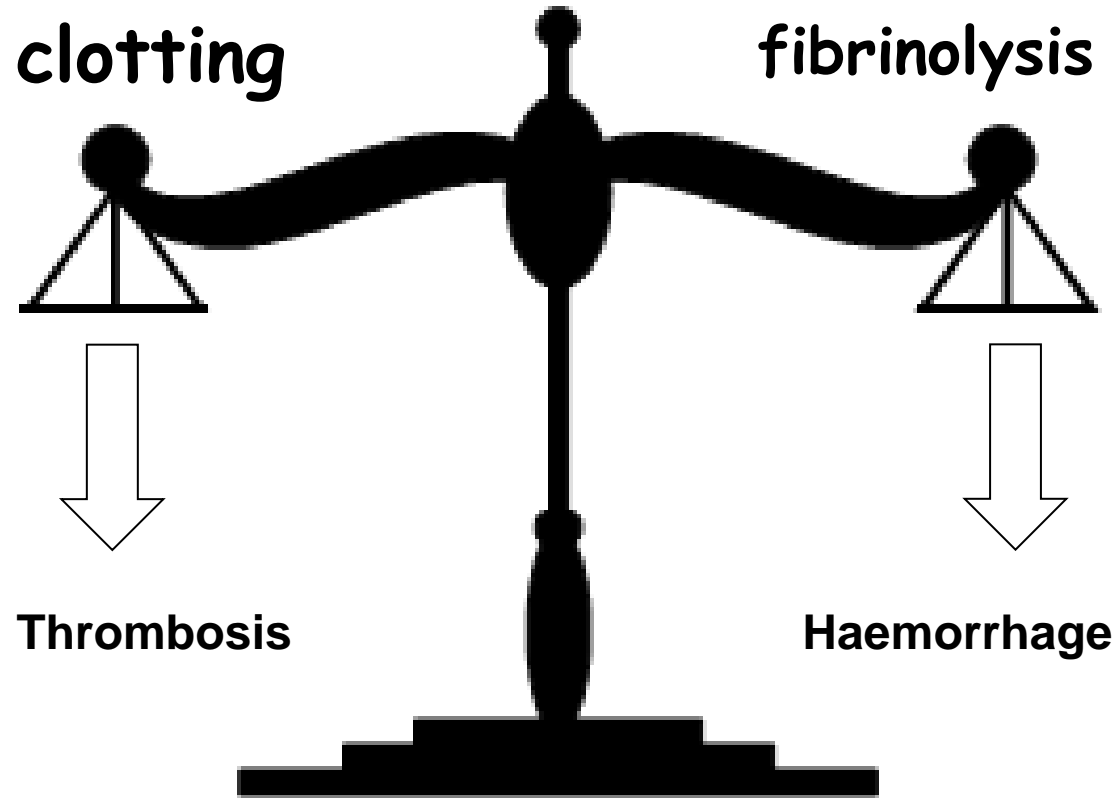
**the spontaneous arrest of bleeding
from ruptured blood vessels**

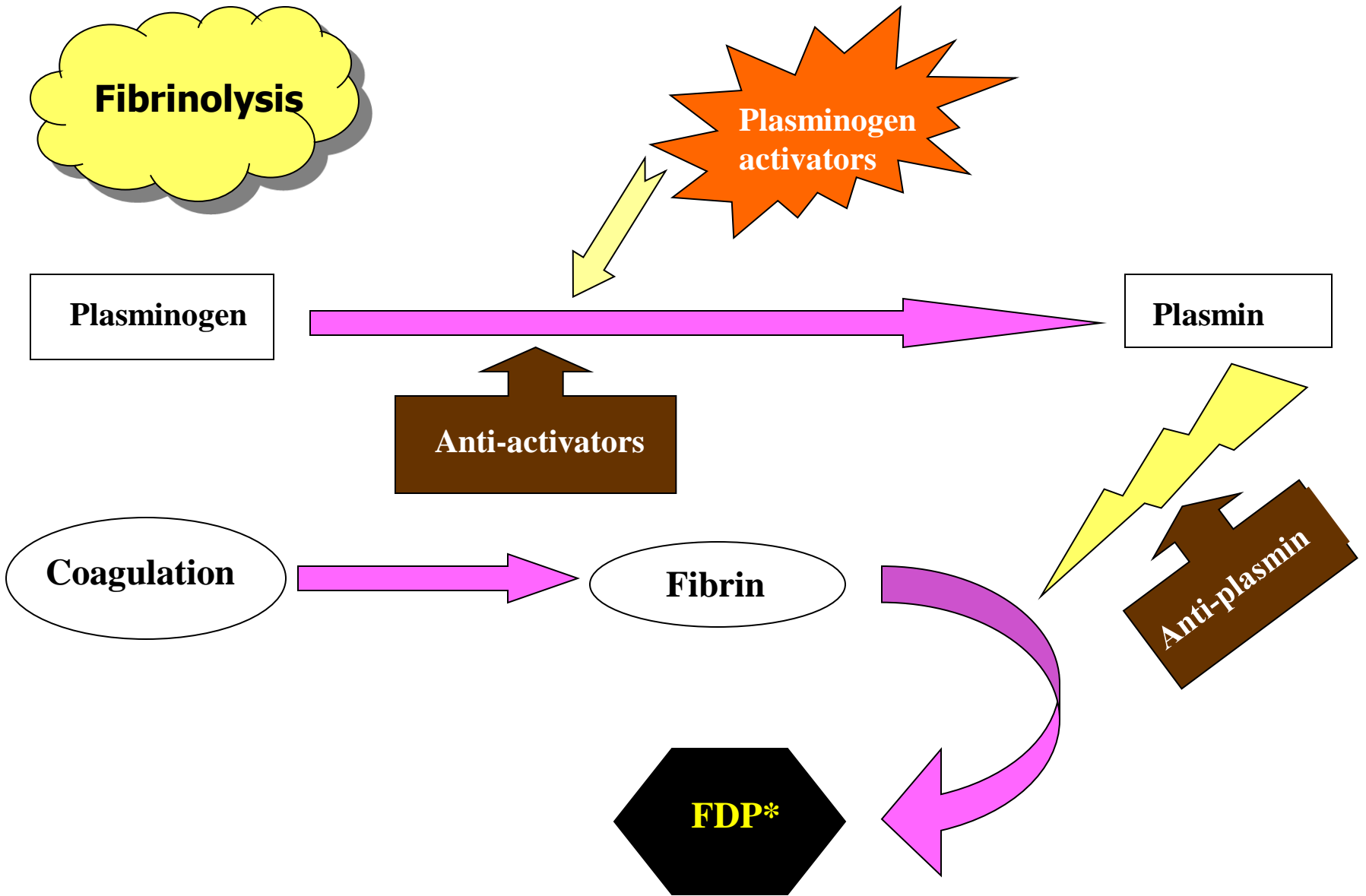
Mechanisms:

- 1. Vessel wall**
- 2. Platelet**
- 3. Blood coagulation**
- 4. Fibrinolytic system (Fibrinolysis)**

Fibrinolysis

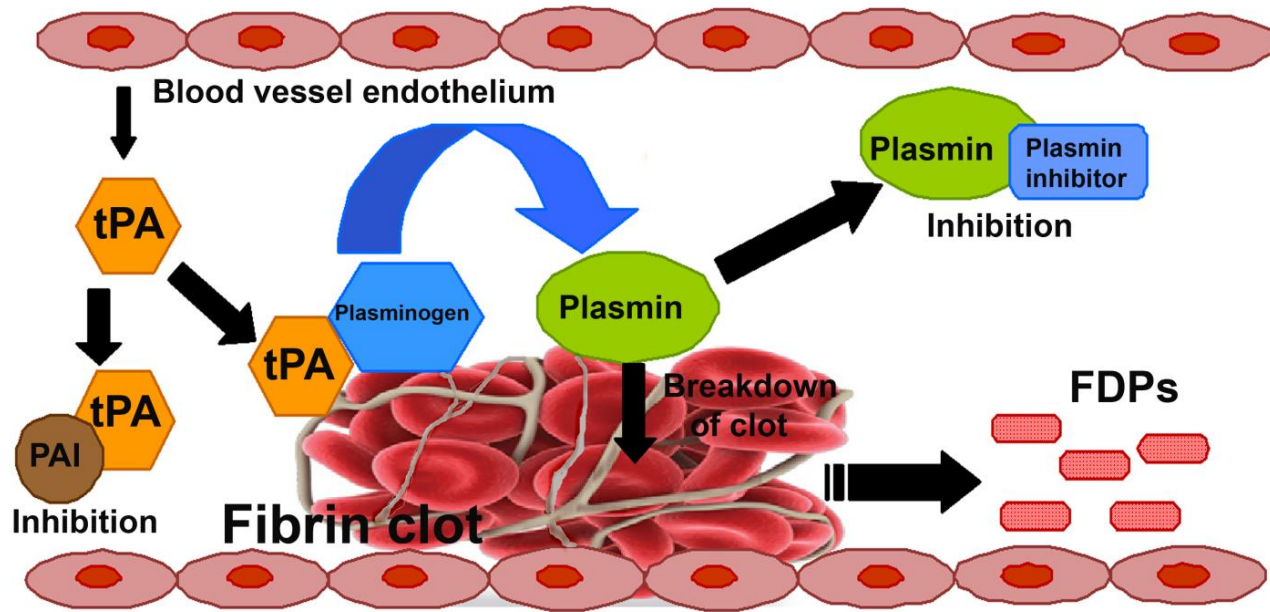
- Formed blood clot can either become fibrous or dissolve
- Fibrinolysis (dissolving) = Break down of fibrin by naturally occurring enzyme plasmin therefore prevent intravascular blocking
- There is balance between clotting and fibrinolysis
 - Excess clotting → blocking of Blood Vessels
 - Excess fibrinolysis → tendency for bleeding



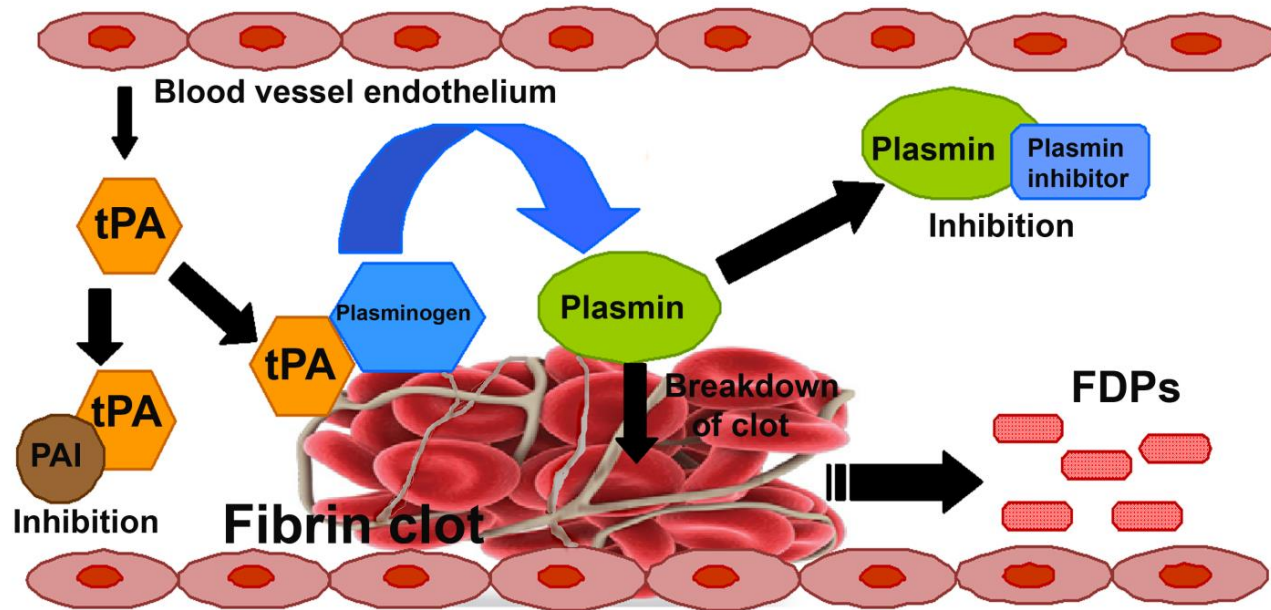


The fibrinolytic System

FDP*: Fibrin Degradation Products

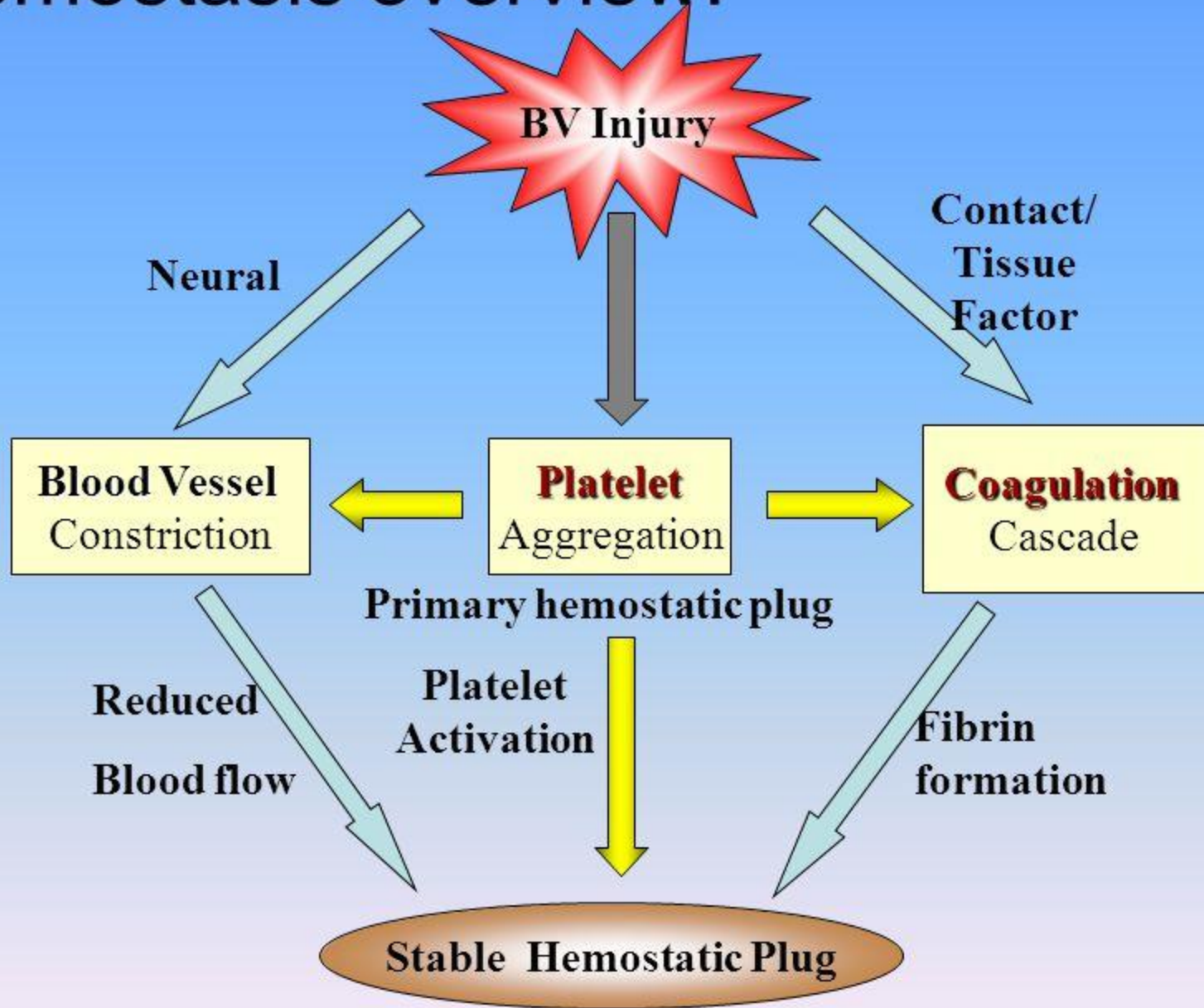


- Plasmin is present in the blood in inactive form plasminogen
- Plasmin is activated by tissue plasminogen activators (t-PA) in blood.
- Plasmin digest intra & extra vascular deposit of Fibrin → fibrin degradation products (FDP)
- Unwanted effect of plasmin is the digestion of clotting factors

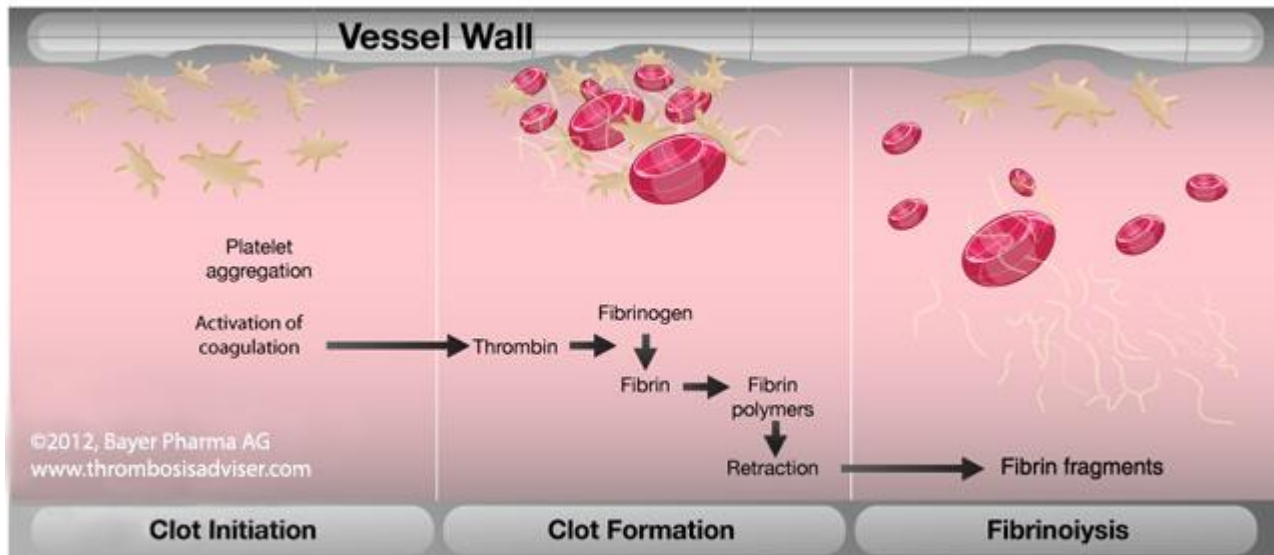


- Plasmin is controlled by:
 - Plasminogen Activator Inhibitor (PAI)
 - Antiplasmin from the liver
- Uses:
 - Tissue Plasminogen Activator (t-PA) used to activate plasminogen to dissolve coronary clots

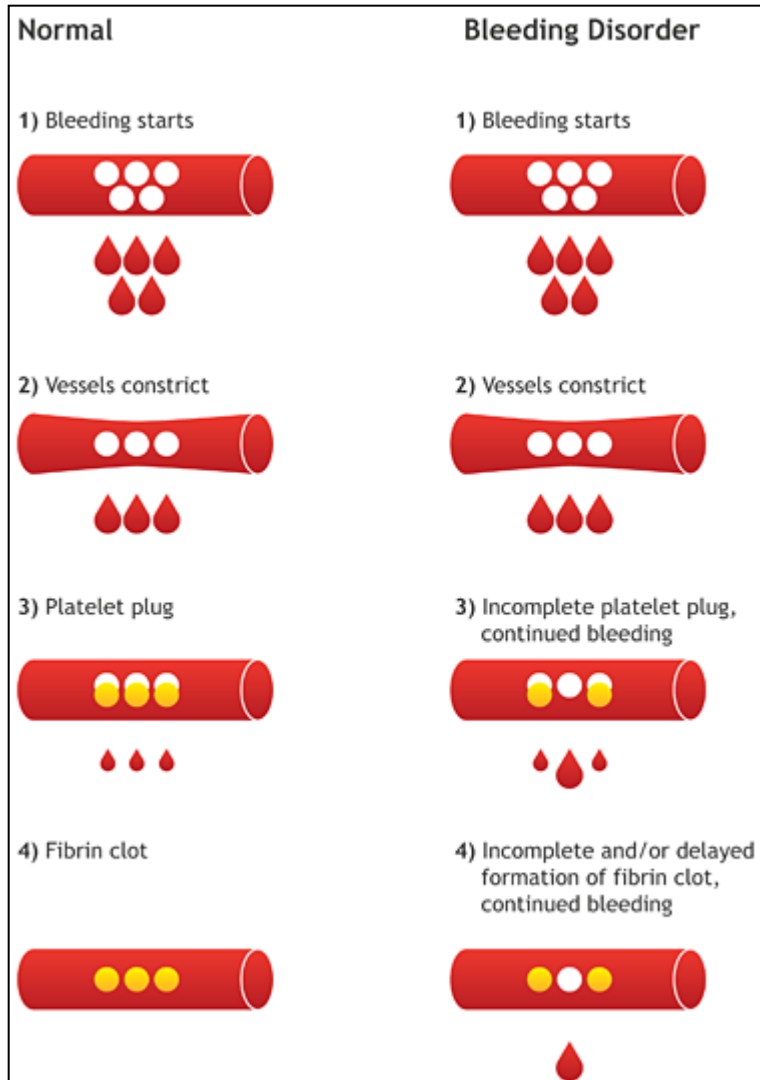
Haemostasis overview:



Haemostatic Mechanisms



Bleeding disorders



- Excessive bleeding can result from:
 - Platelet defects: deficiency in number (thrombocytopenia) or defect in function.
 - Coagulation factors defect: Deficiency in coagulation factors (e.g. hemophilia).
 - Vitamin K deficiency.

Cont. bleeding disorders

- Hemophilia:
 - ↑ bleeding tendency.
 - X-linked disease.
 - Affects males.
 - 85% due to FVIII deficiency (hemophilia A), and 15% due to FIX deficiency (hemophilia B).
- Vitamin K deficiency & liver disease:
 - Almost all coagulation factors are synthesized in the liver.
 - Prothrombin, FVII, FIX, & FX require vitamin K for their synthesis.



THANK YOU