Haemostasis

TEXTBOOK OF MEDICAL PHYSIOLOGY

GUYTON & HALL 11TH EDITION

UNIT VI CHAPTER 36

Dr.Mohammed Alotaibi

MRes, PhD (Liverpool, England)
Department of Physiology
College of Medicine
King Saud University

Haemostasis *or* Hemostasis

NOT

Homeostasis

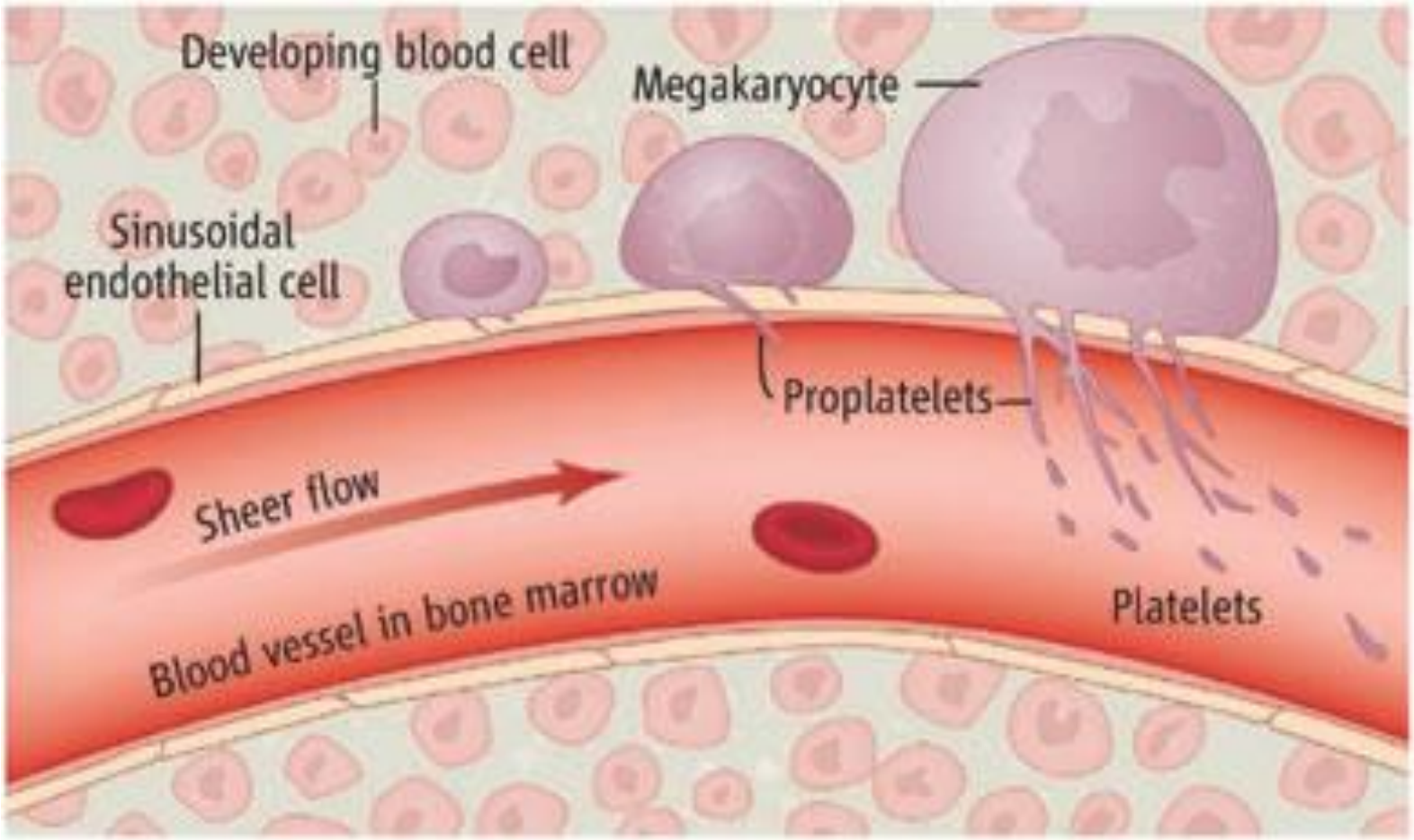
The ability to maintain a constant internal environment in response to environmental changes

Objectives

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

1. Describe the formation and development of platelets
2. Recognize different mechanisms of hemostasis
3. Describe the role of platelets in hemostasis.
4. Recognize different clotting factors
5. Describe the cascades of intrinsic and extrinsic pathways for clotting.
6. Recognize process of fibrinolysis and function of plasmin

Megakayocyte and platelets formation



Platelets – cont.

Site of formation:

(Bone marrow)

Myeloid stem cell

⇩

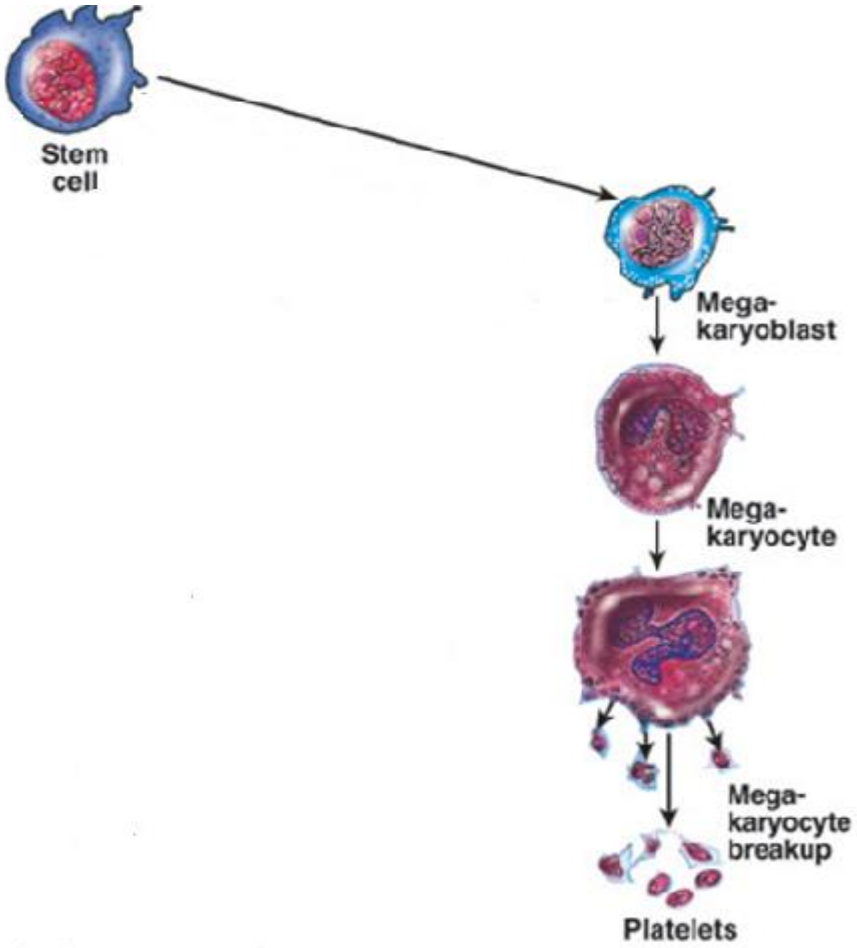
Megakaryoblast

⇩

Megakaryocyte

⇩

Platelets



Platelets (Thrombocytes)

They are fragments of **megakaryocytes** formed in the bone marrow. Their production (thrombopoiesis) is regulated by **Thrombopoietin**, a hormone released from the liver

Platelets - cont

- Are round/oval disc with diameter about 2-3 µm
- Coated by a glycoprotein layer which prevents their sticking to normal endothelial cells
- Platelet count = 250,000-500,000/ mm^3
- life span 8-12 days
- Active cells contain contractile protein such as actin, myosin, and thrombosthenin
- Contain high calcium content & rich in ATP

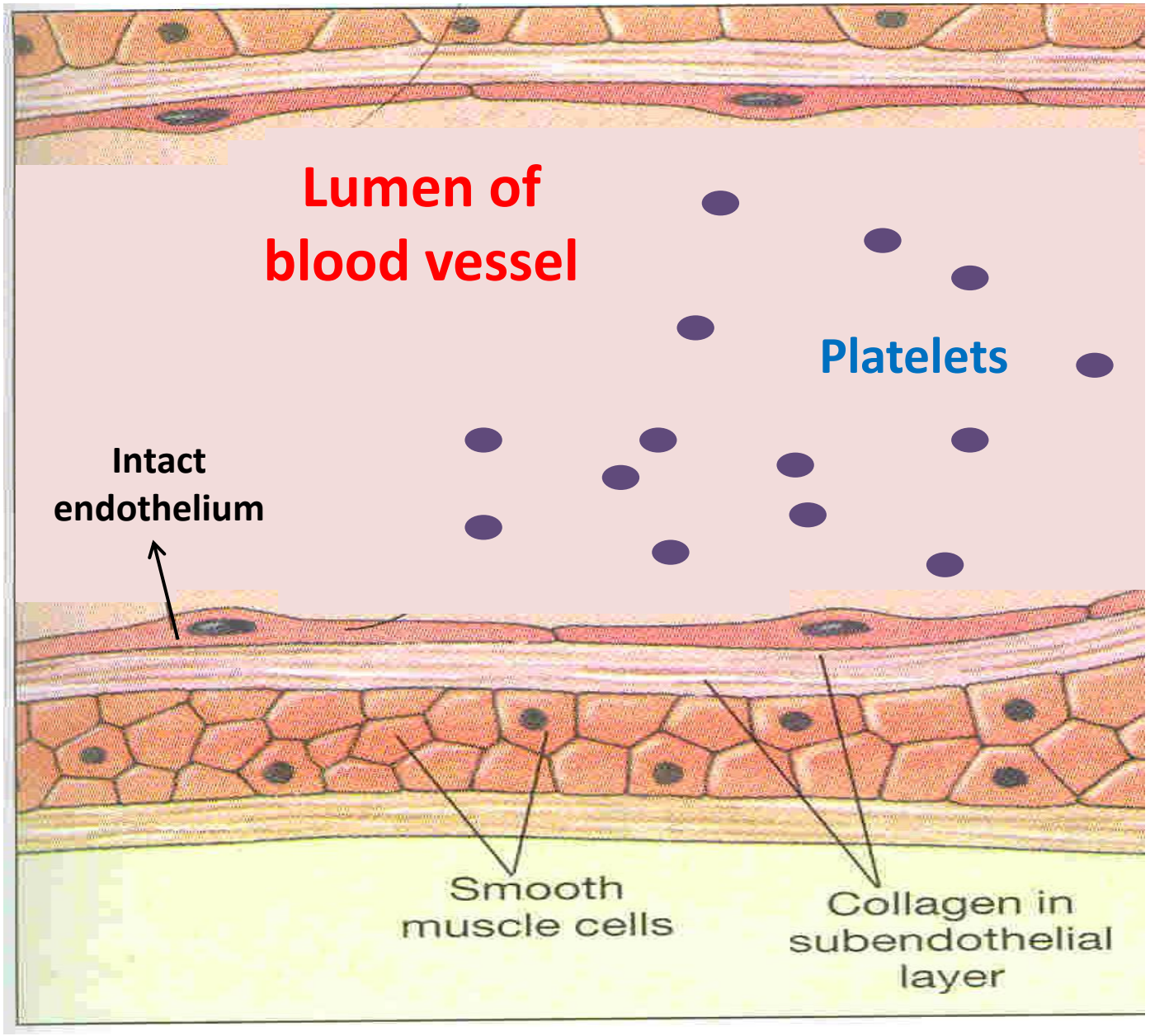
Hemostasis:

prevention or stoppage of blood loss.

Hemostatic Mechanisms:

1. **Vessel wall** (Vasoconstriction)
2. **Platelets** (Production and activation, Platelets Plug formation)
3. **Blood coagulation**

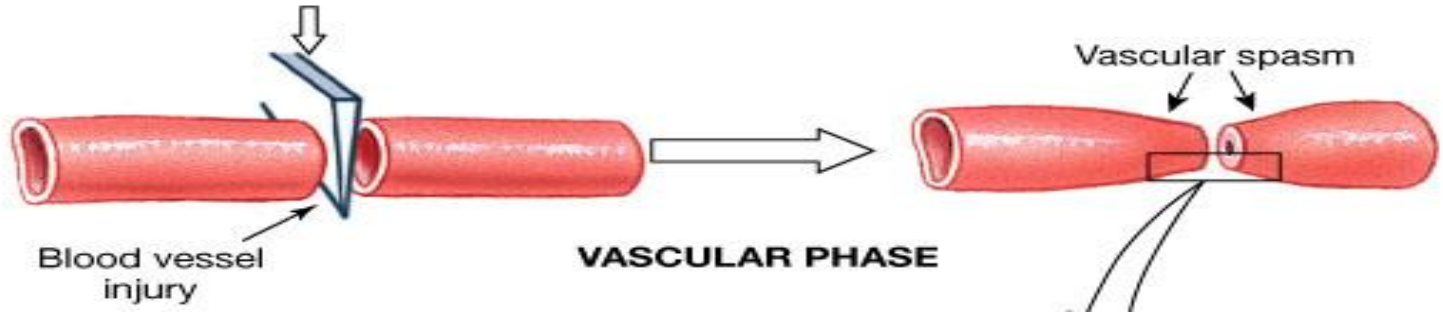
   Clot formation (intrinsic & extrinsic pathways)
4. **Fibrinolysis**


Lumen of blood vessel
Platelets
Intact endothelium
Smooth muscle cells
Collagen in subendothelial layer

Memostatic Mechanisms

Vessel wall

- Immediately After injury a localized **Vasoconstriction** of smooth muscles



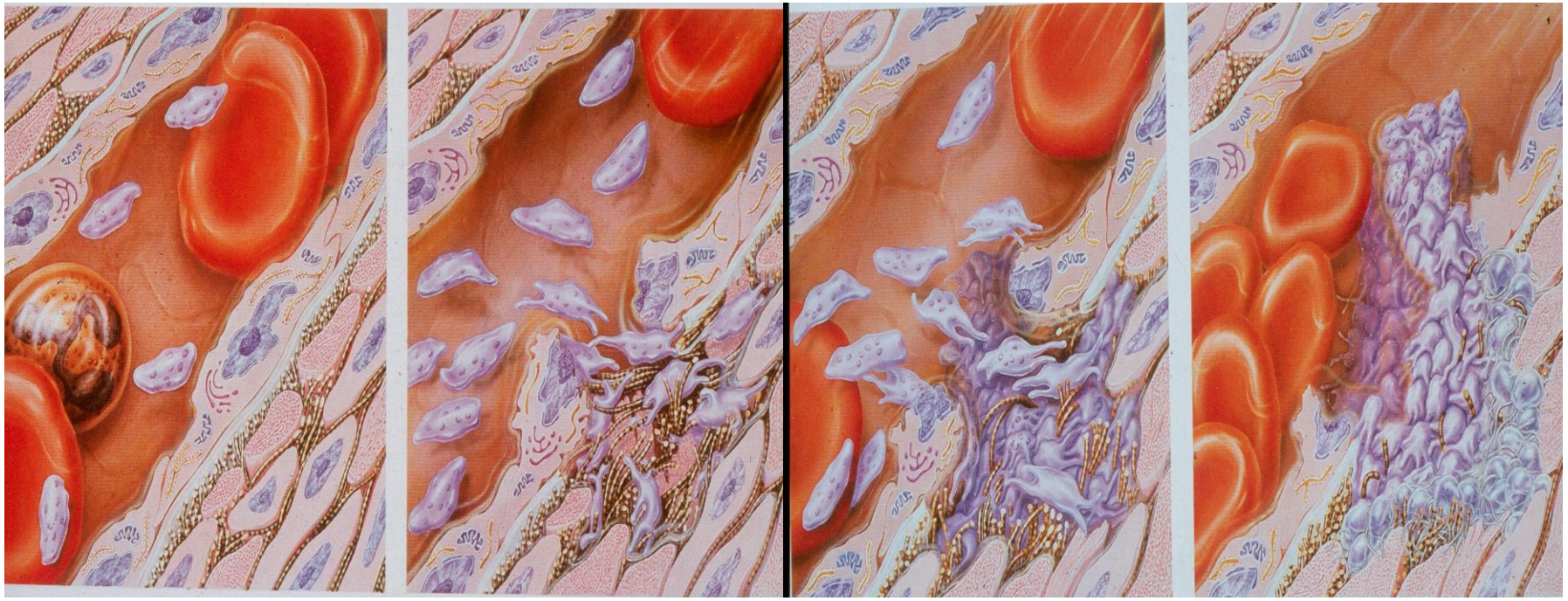
– Mechanism

-Hurmonal factors:

- local release of thromboxane A2 & serotonin (5HT) from platelets
- Systemic release of adrenaline

- Nervous reflexes (pain nerve impulses)

Platelet plug formation



Platelet Functions

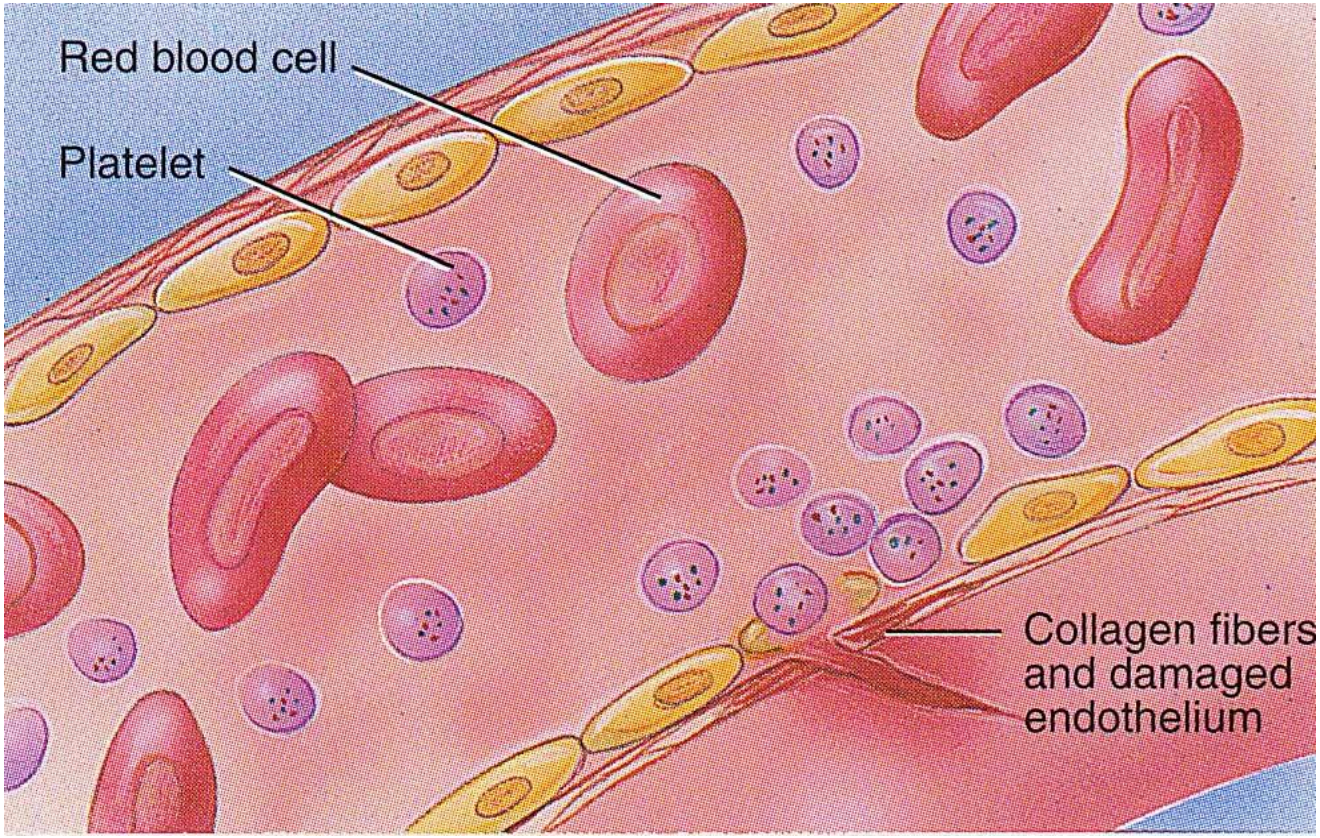
Begins with Platelet activation

Platelet Activation

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

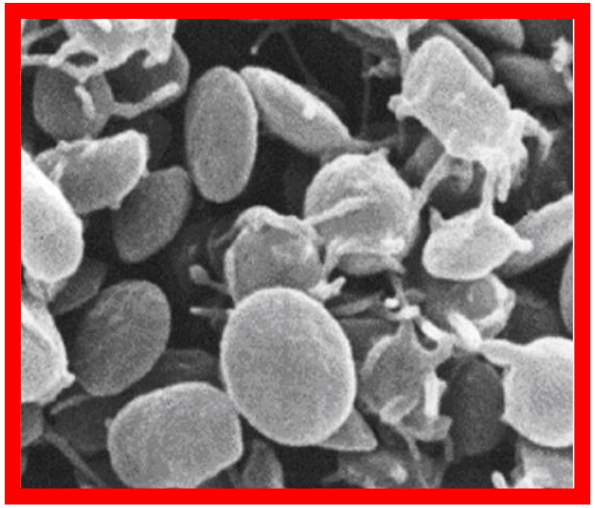
Platelet Adhesion

- Platelets stick to the exposed collagen underlying damaged endothelial cells in vessel wall

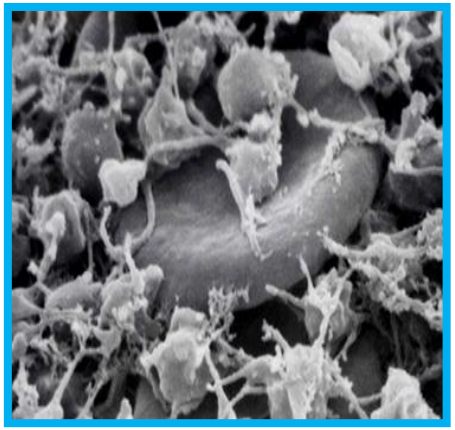


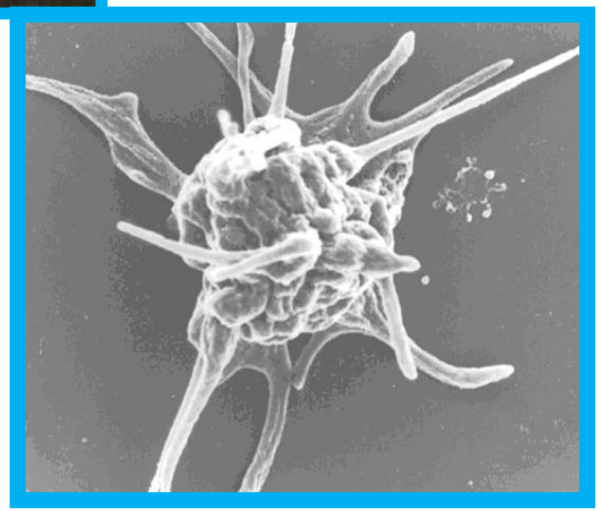
Platelet shape change and Aggregation

Resting platelet



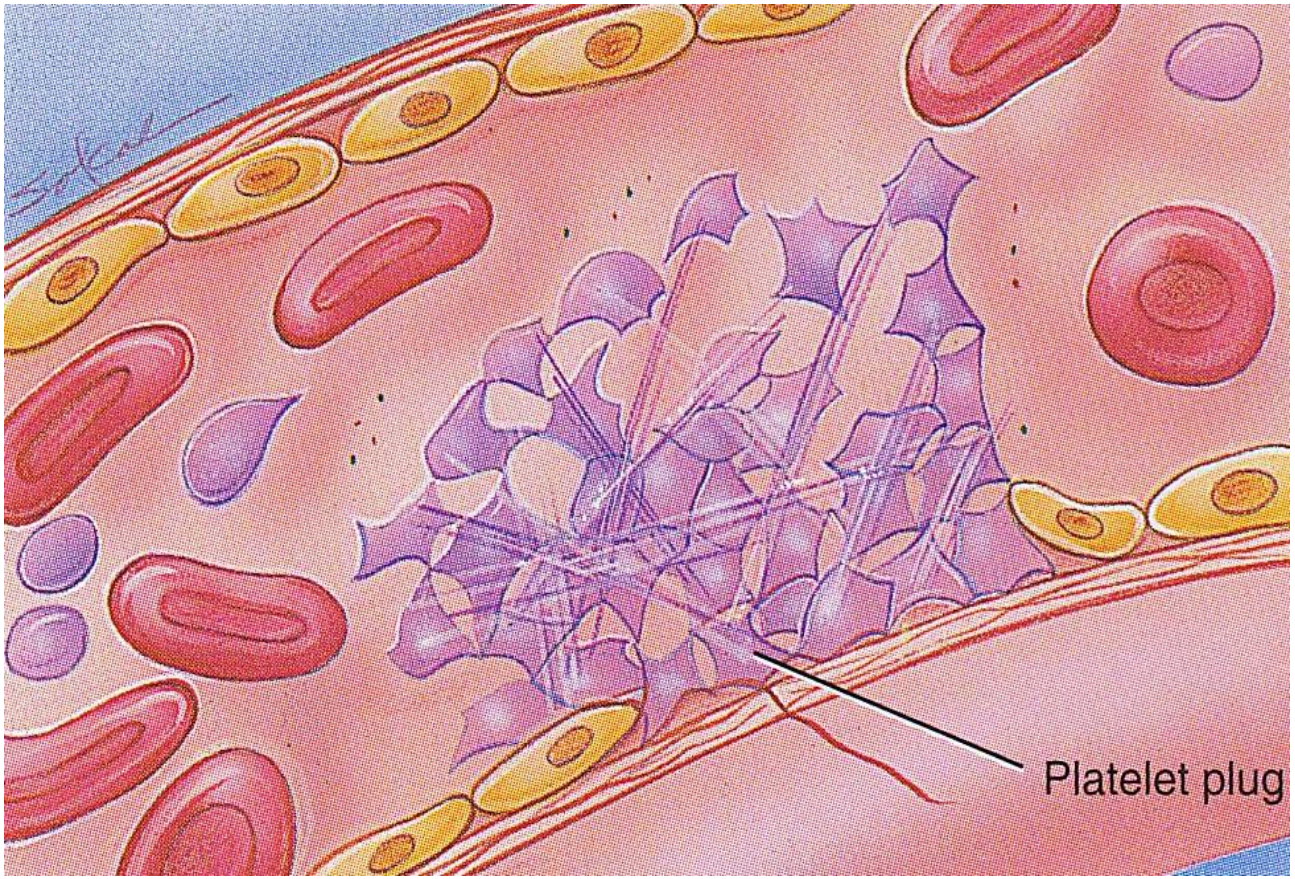
Activated platelet





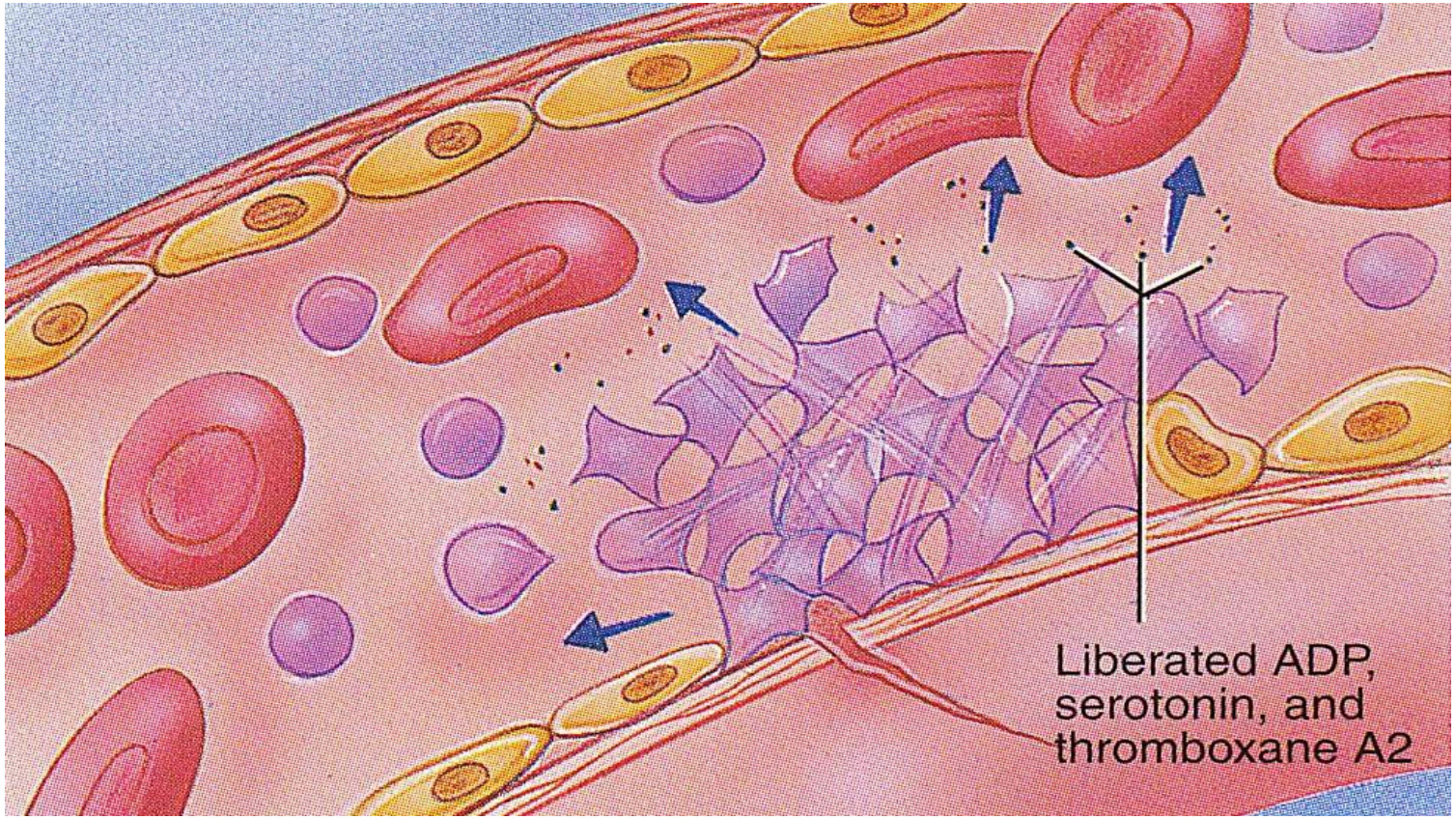
Platelet Aggregation

- 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

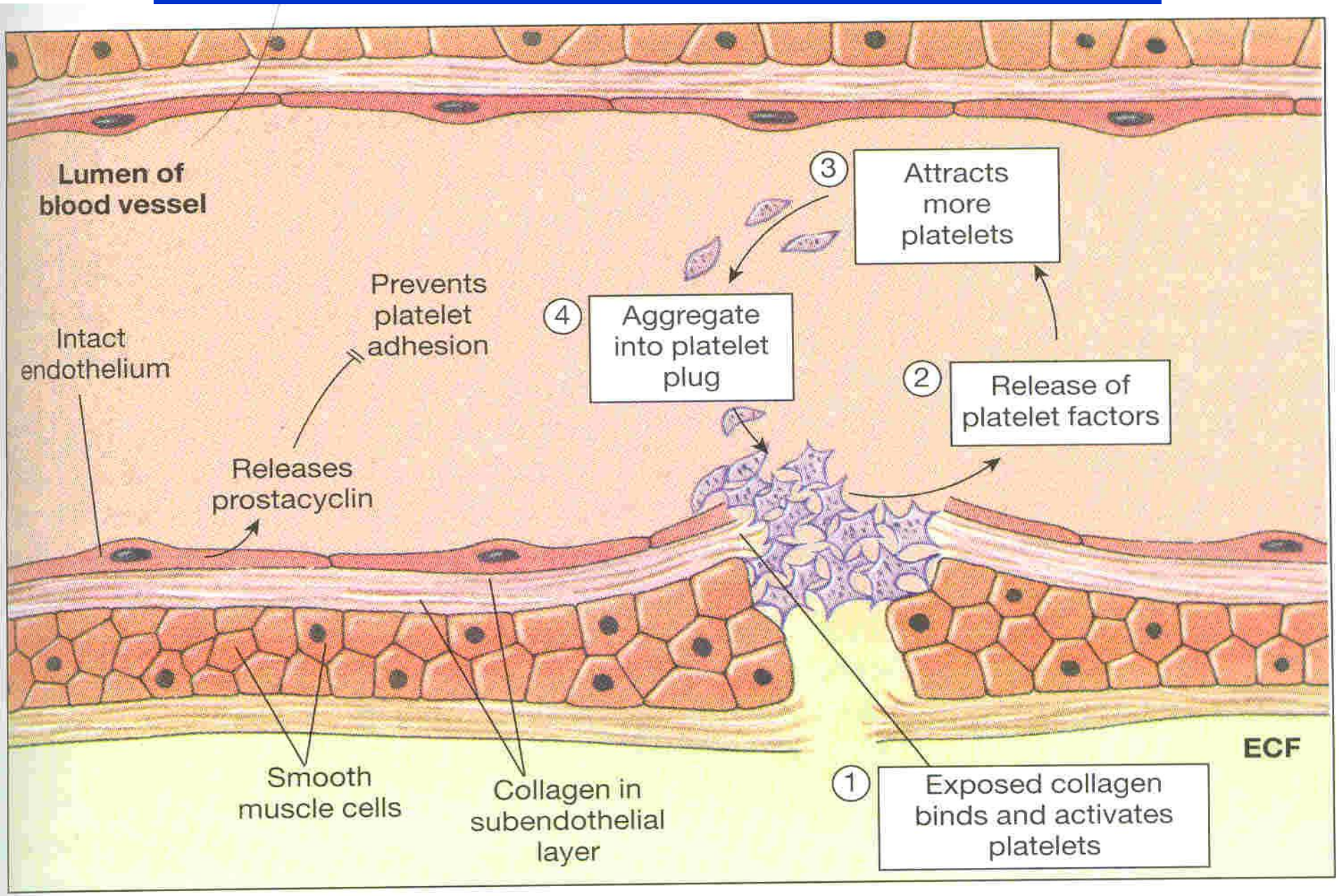


Platelet Release Reaction

- 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



Platelet plug formation



Platelet Plug

Aggregation of platelets at the site of injury to stop bleeding

- Exposed collagen attracts platelets
- Activated platelets release ADP & Thromboxane A2 (TXA2) → ↑ the stickiness of platelets → ↑ Platelets aggregation → plugging of the cut vessel
- Intact endothelium secretes prostacyclin → inhibition of aggregation

Activated Platelets

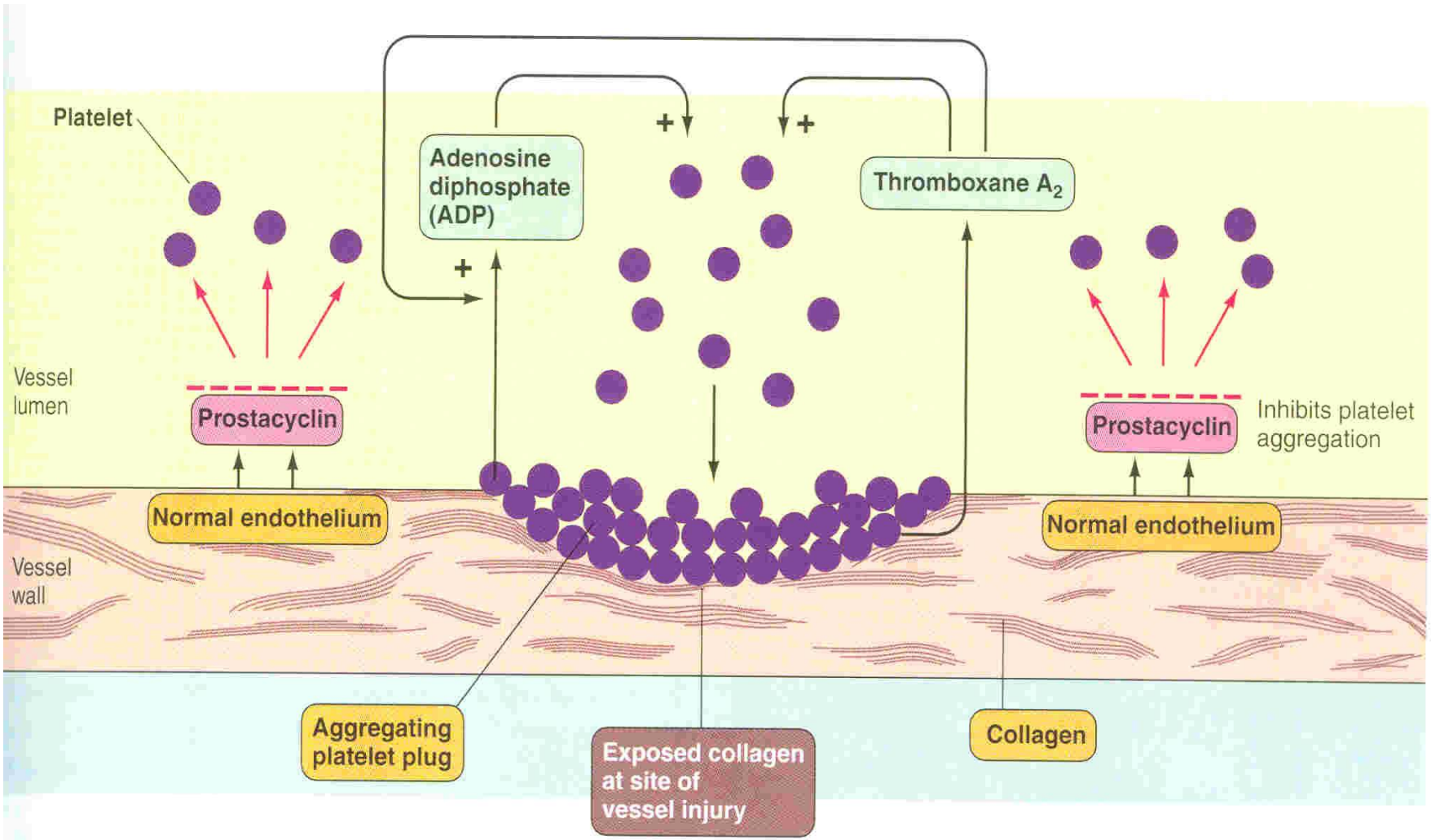
Secrete:

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

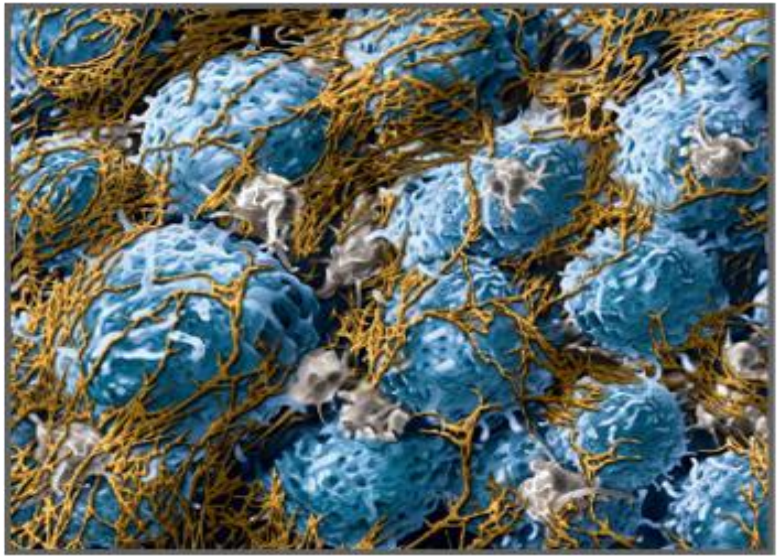
   Function:

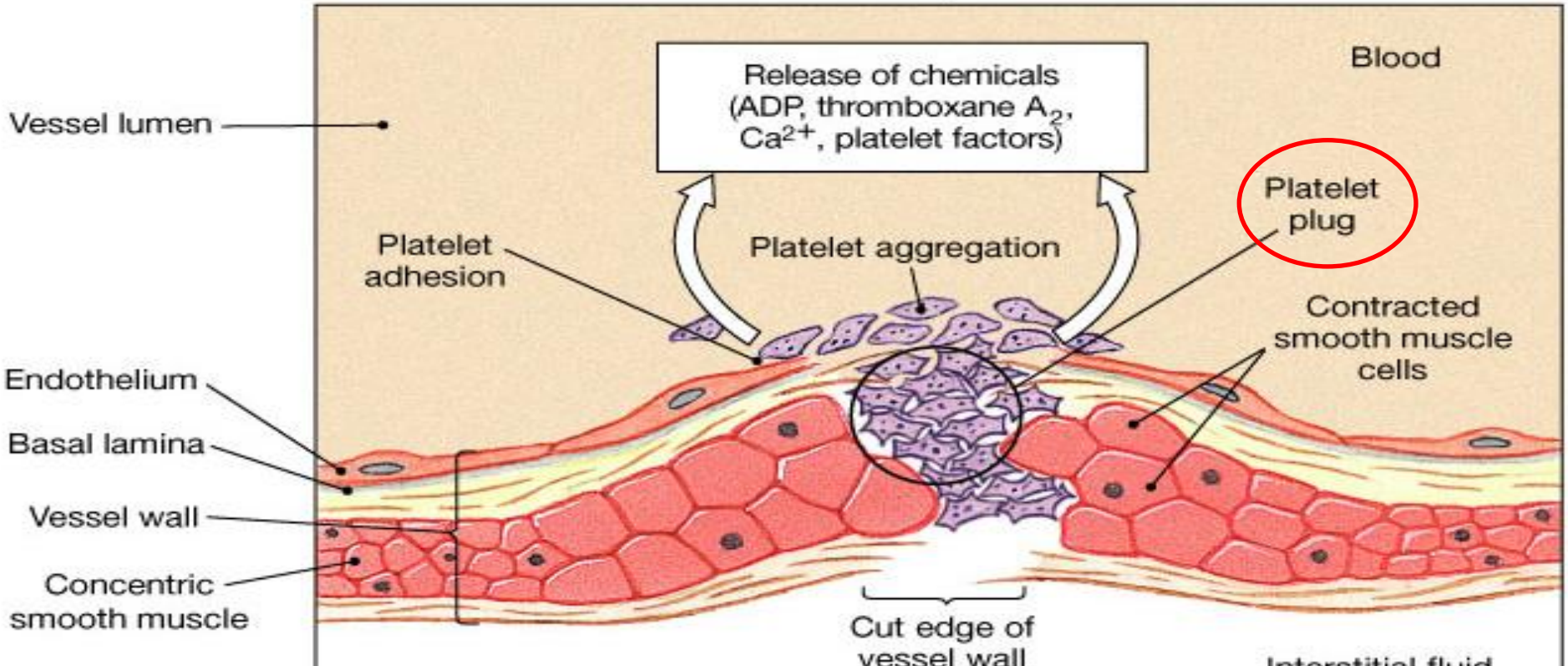
   - Vasoconstriction
   - Platelet aggregation

   (TXA2 inhibited by aspirin)


Platelet
Adenosine diphosphate (ADP)
+
+
+
Thromboxane A_2
Vessel lumen
Prostacyclin
Normal endothelium
Vessel wall
Prostacyclin
Inhibits platelet aggregation
Normal endothelium
Aggregating platelet plug
Exposed collagen at site of vessel injury
Collagen

Coagulation: Formation of fibrin meshwork (Threads) to form a CLOT

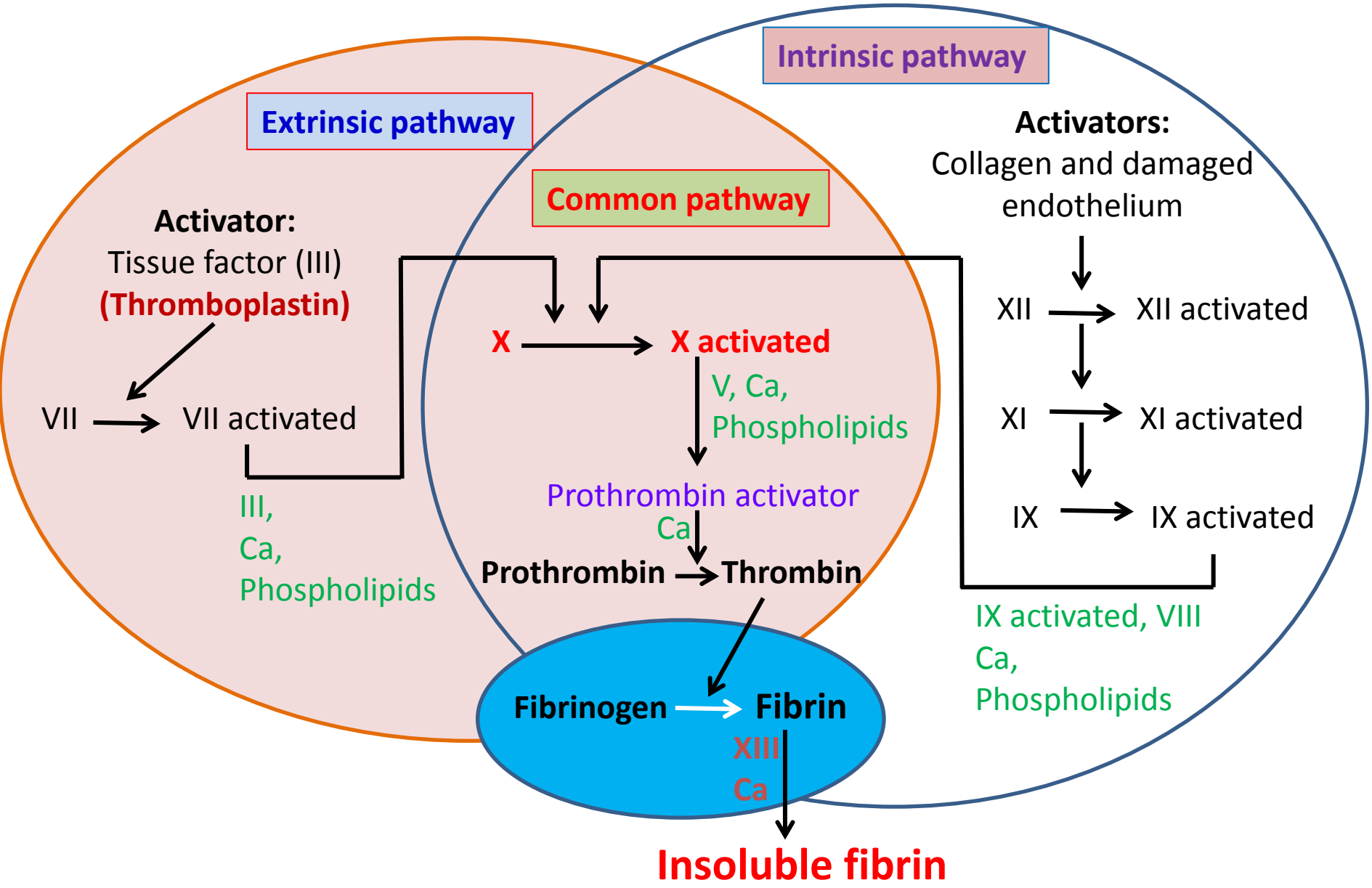




Clotting Factors

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

The Coagulation Cascades



Blood coagulation
(clot formation)

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

Intrinsic pathway

- The trigger is the activation of factor XII by contact with foreign surface, injured blood vessel, and glass.
- Activated factor XII will activate factor XI
- Activated factor Xl will activate IX
- Activated factor IX + factor VIII + platelet phospholipid factor (PF3)+ Ca activate factor X
- Following this step the pathway is common for both intrinsic and extrinsic

Extrinsic pathway

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

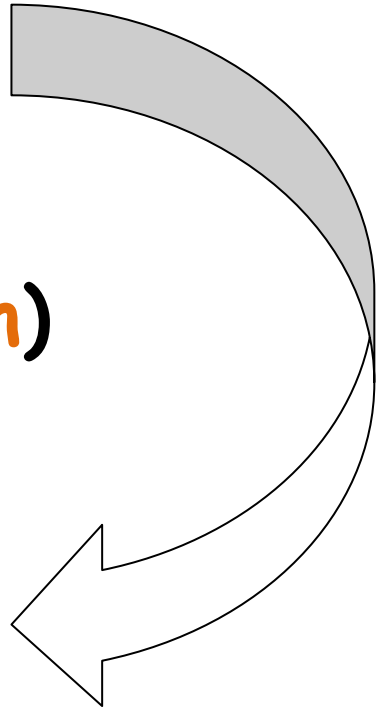
Common pathway

- Activated factor X + factor V +PF3 + Ca activate prothrombin activator; a proteolytic enzyme which activates prothrombin.
- Activated prothrombin activates thrombin
- Thrombin acts on fibrinogen and change it into insoluble thread like fibrin.
- Factor XIII + Calcium → strong fibrin (strong clot)

Activation of Blood Coagulation

- **Intrinsic Pathway:** all clotting factors present in the blood

- **Extrinsic Pathway:** triggered by tissue factor (thromboplastin)



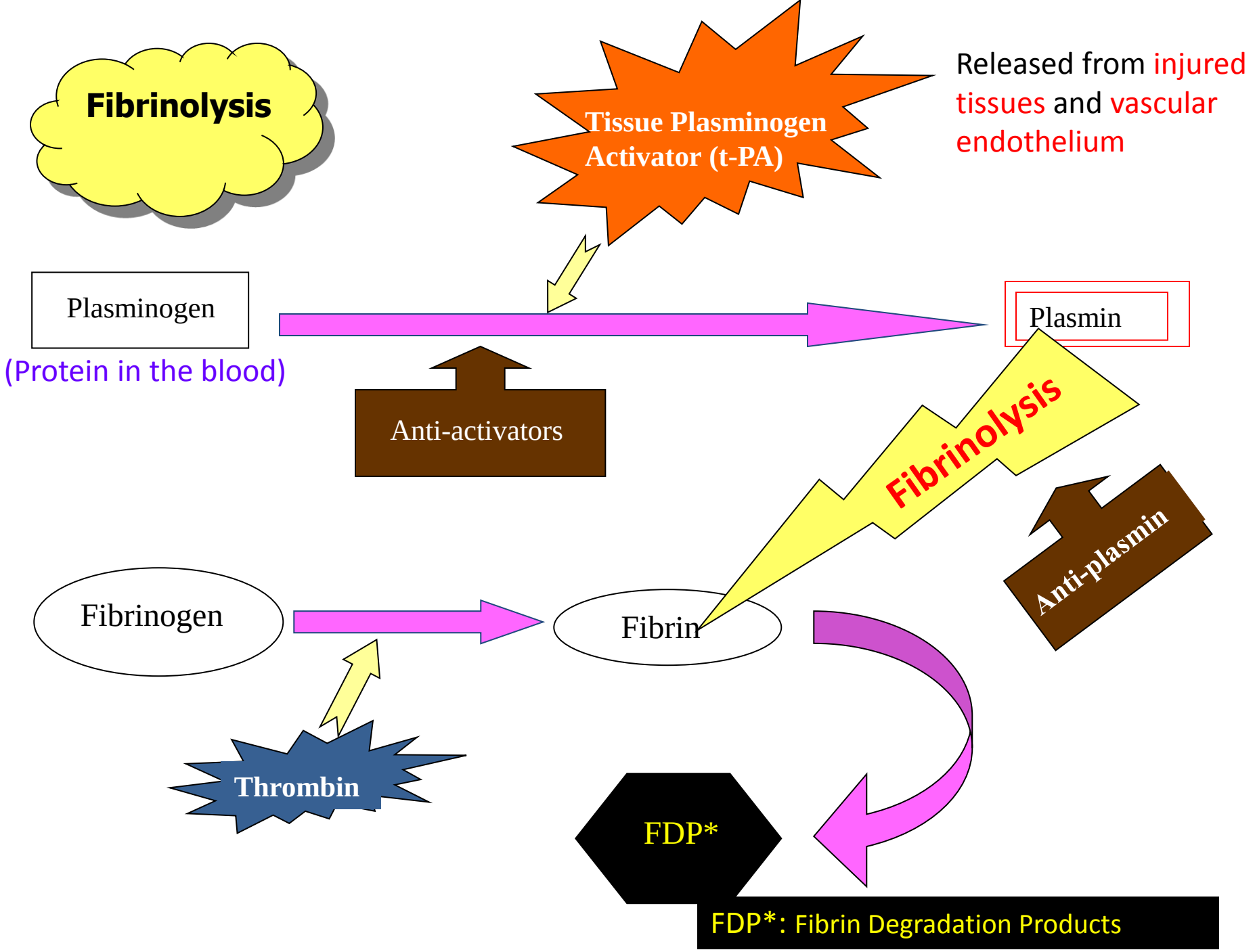
Common Pathway

Thrombin

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

Fibrinolysis

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


Fibrinolysis
Tissue Plasminogen Activator (t-PA)
Released from injured tissues and vascular endothelium
Plasminogen
(Protein in the blood)
Plasmin
Anti-activators
Fibrinolysis
Anti-plasmin
Fibrinogen
Fibrin
Thrombin
FDP*
FDP*: Fibrin Degradation Products

Plasmin

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

Plasmin

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