Blood Physiology

Haemostasis

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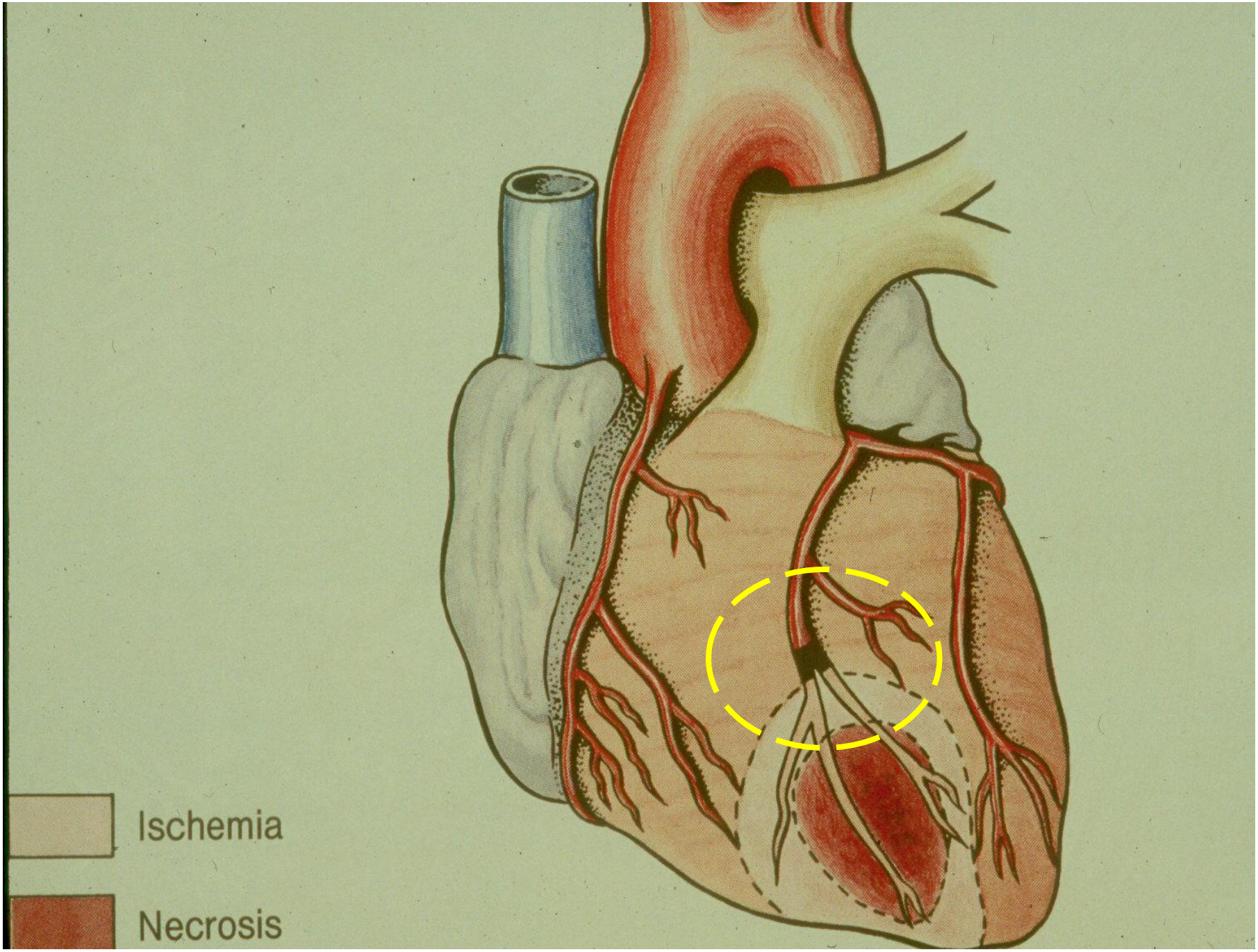
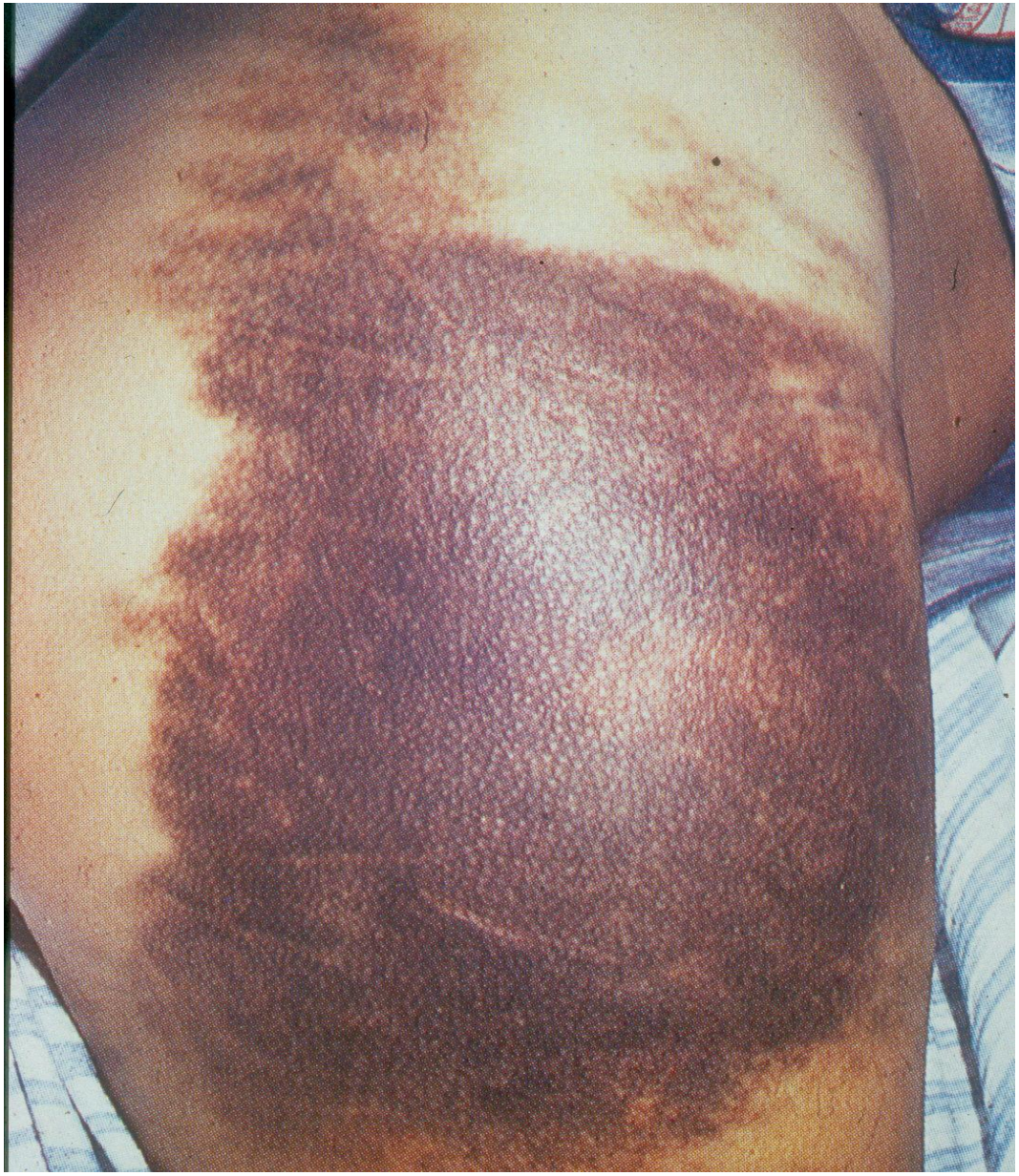
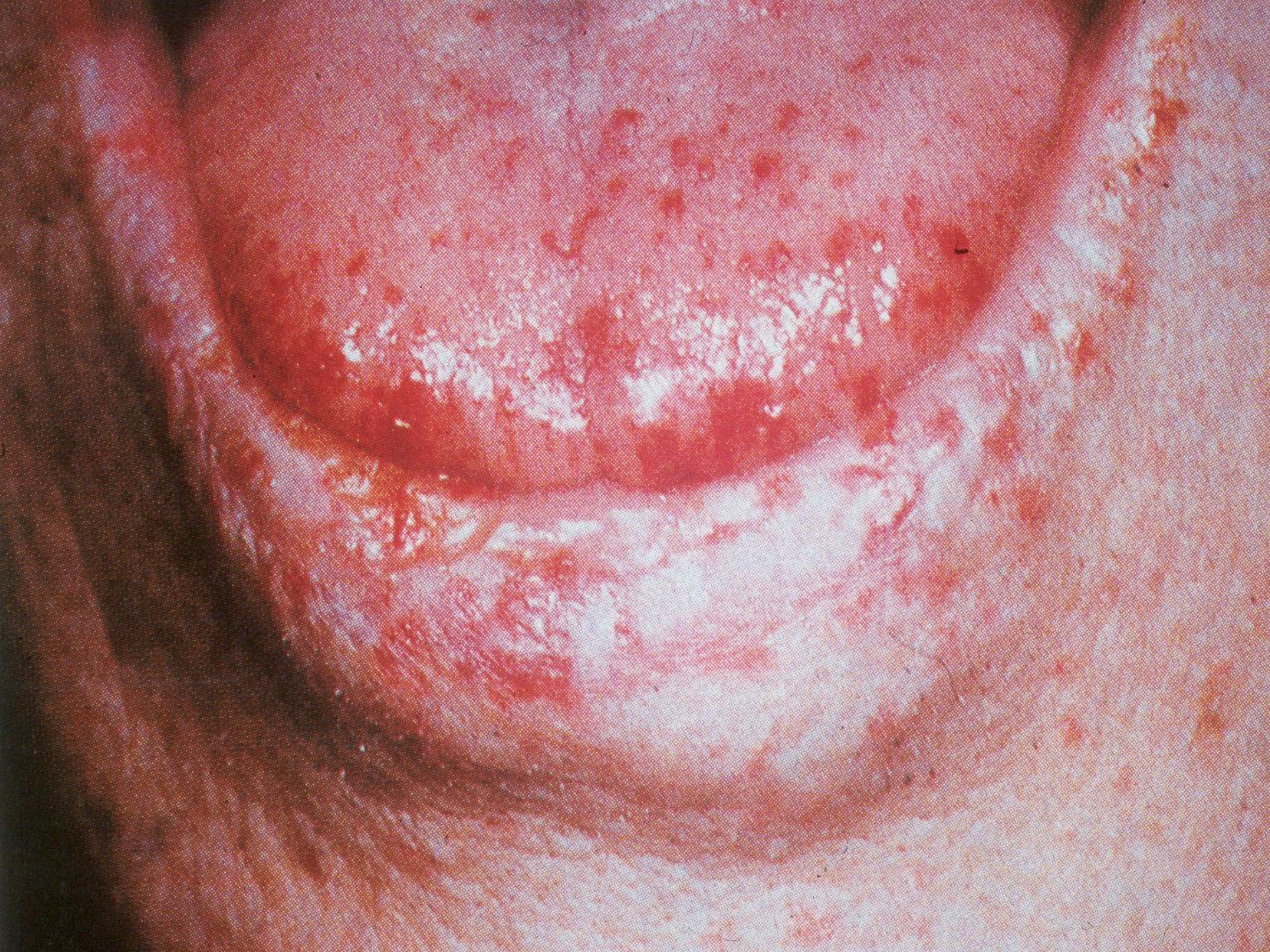

Ischemia
Necrosis





Objectives

At the end of this lecture you 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 .

Objectives - cont.

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

Topics

1. Haemostasis (Definition).
2. Capillaries vasoconstriction.
3. Platelets synthesis and function
4. Platelets Plug.
5. Clot formation (intrinsic & exterinsic pathway) and function of thrombin.
6. Fibrinolysis and plasmin.

Haemostasis

Hemostatic Mechanisms

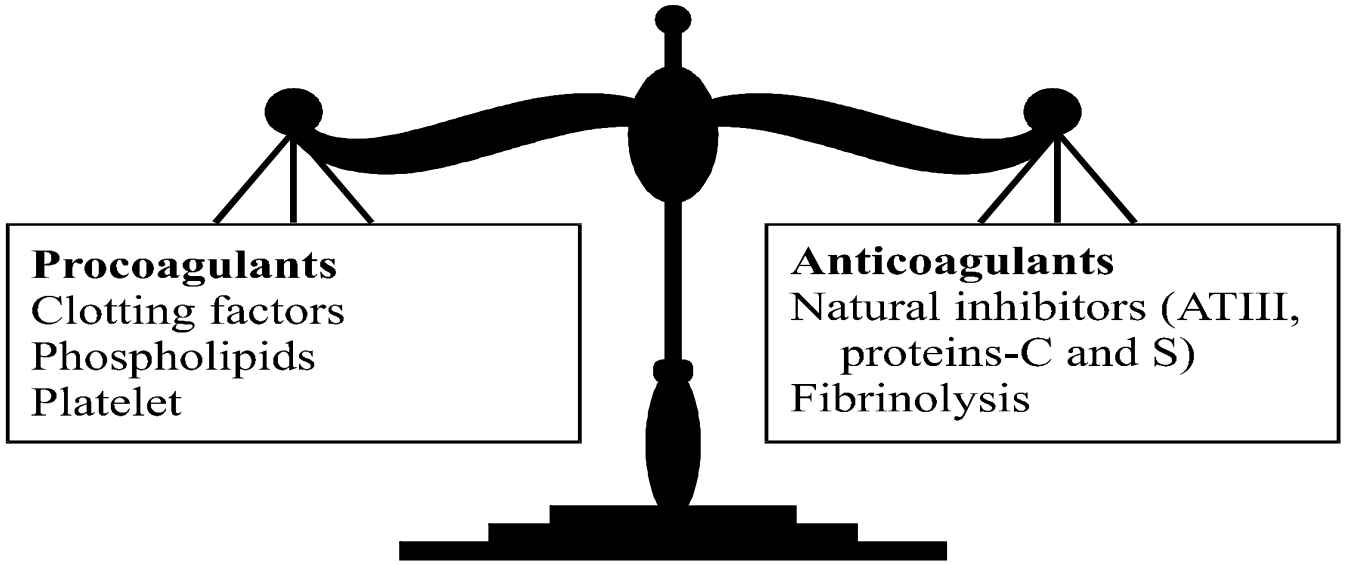
1. **Vessel wall (Vasoconstriction)**
2. **Platelets** (Production and function, Platelets Plug formation)
3. **Blood Coagulation mechanism**
   Clot formation (intrinsic & extrinsic pathways)

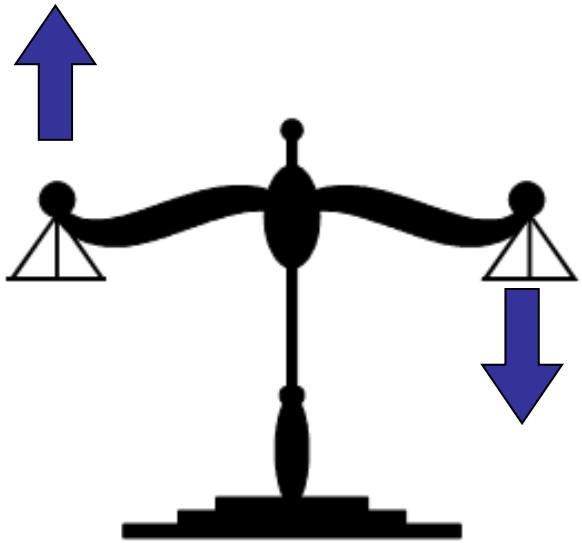
4. (Fibrinolysis)

Homeostasis of the clotting system.

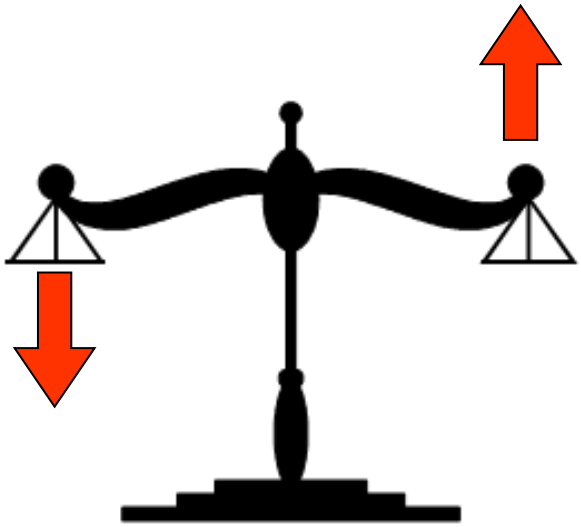
- **A crucial physiological balance exists between factors favouring clotting (procagulants) and factors that oppose it (anticoagulants).**

- **Disturbances in this balance can lead to thrombosis or bleeding.**





Thrombosis



Haemorrhage

Hemostasis:

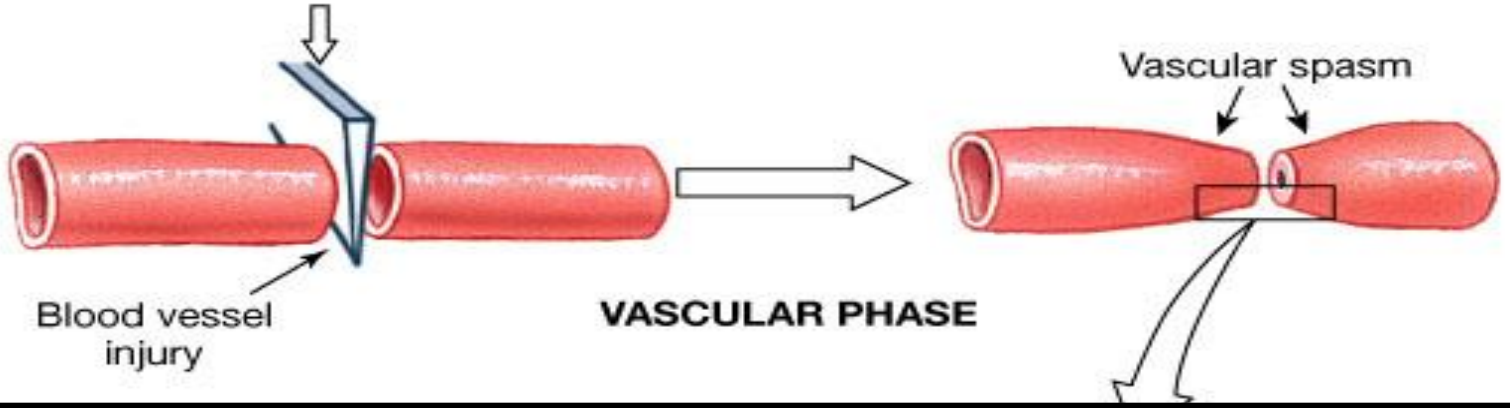
the spontaneous arrest of bleeding from ruptured blood vessels

Mechanisms:

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

Hemostatic Mechanisms:

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


Vascular spasm
Blood vessel injury
VASCULAR PHASE

Hemostatic Mechanisms- cont

1. Vessel wall

- Immediately After injury a localized. **Vasoconstriction.**

Mechanism:

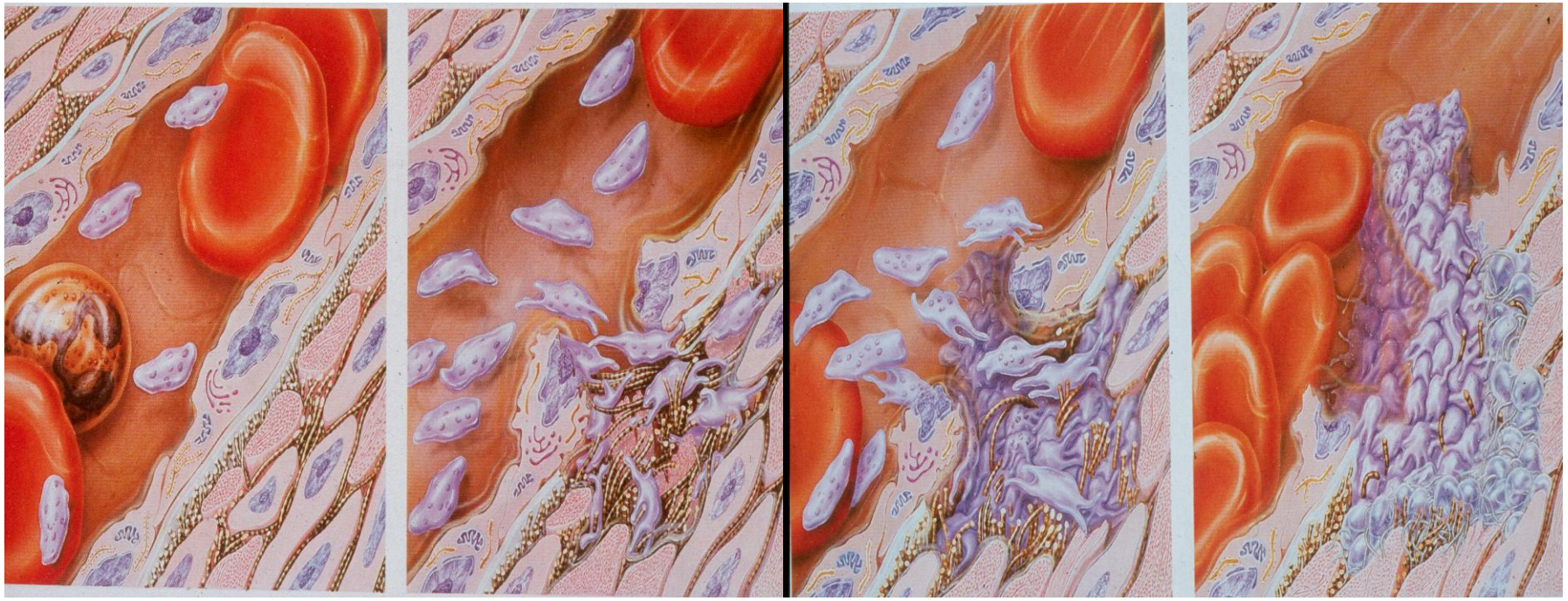
-Hurmoral factors.

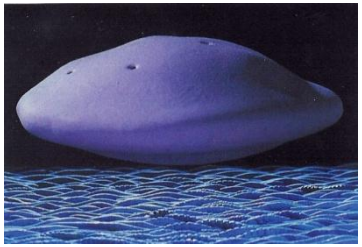
- local release of thromboxane A2 & 5HT by platelets.
- Systemic release of adrenaline.

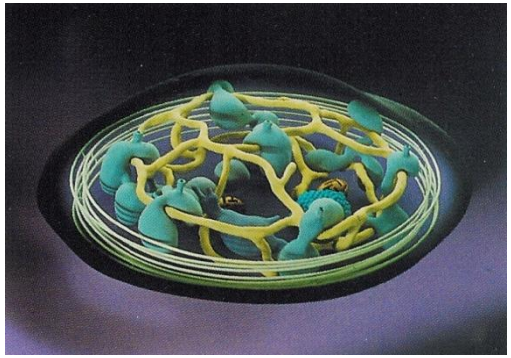
- Nervous factors.

Hemostatic Mechanisms:

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





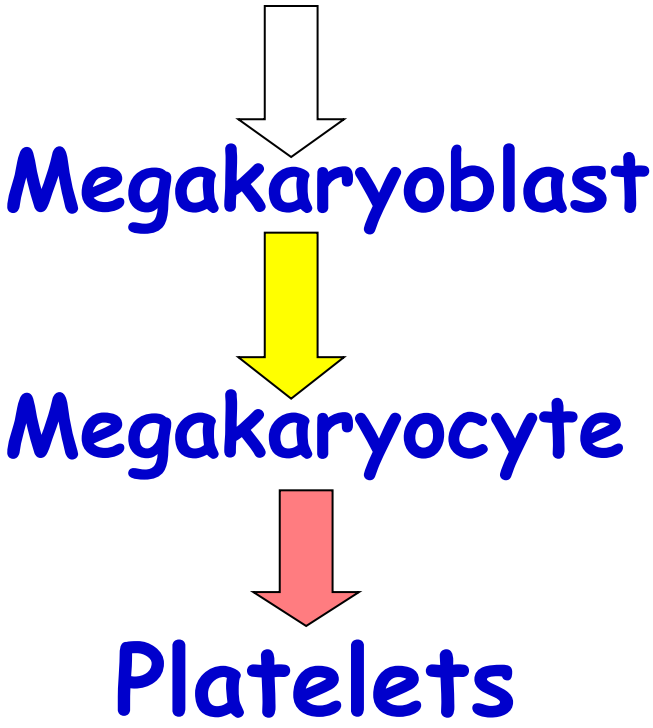


Platelets – cont.

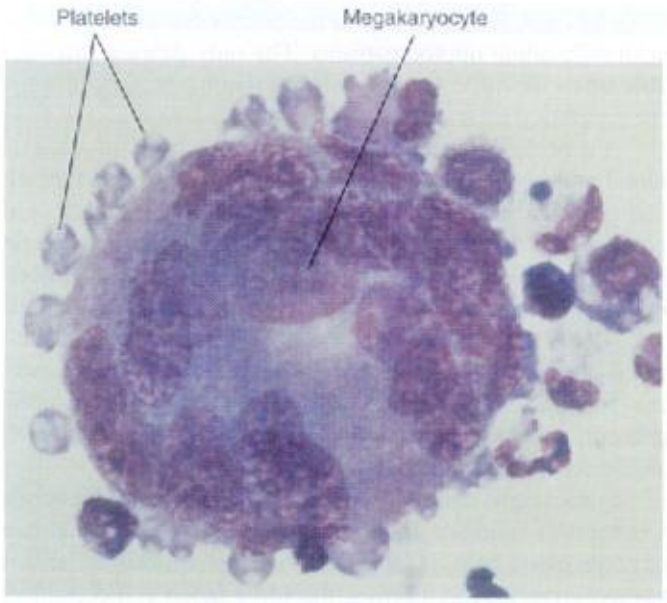
Site of formation:

Bone marrow

Steps: Stem cell



Megakayocyte and platelet formation



Platelets

Thrombocytes are

- Fragments of megakaryocytes in the bone marrow

- Platelet count = $150x10^3$-$300x10^3$/ml,
- life span 8-12 days
- Active cells contain contractile protein,
- Contain high calcium content & rich in ATP

Platelets Formation (Thrombopoiesis)

Regulation of thrombopoiesis by Thrombombopoietin

Platelet Functions

Begins with Platelet activation

Platelets Functions:

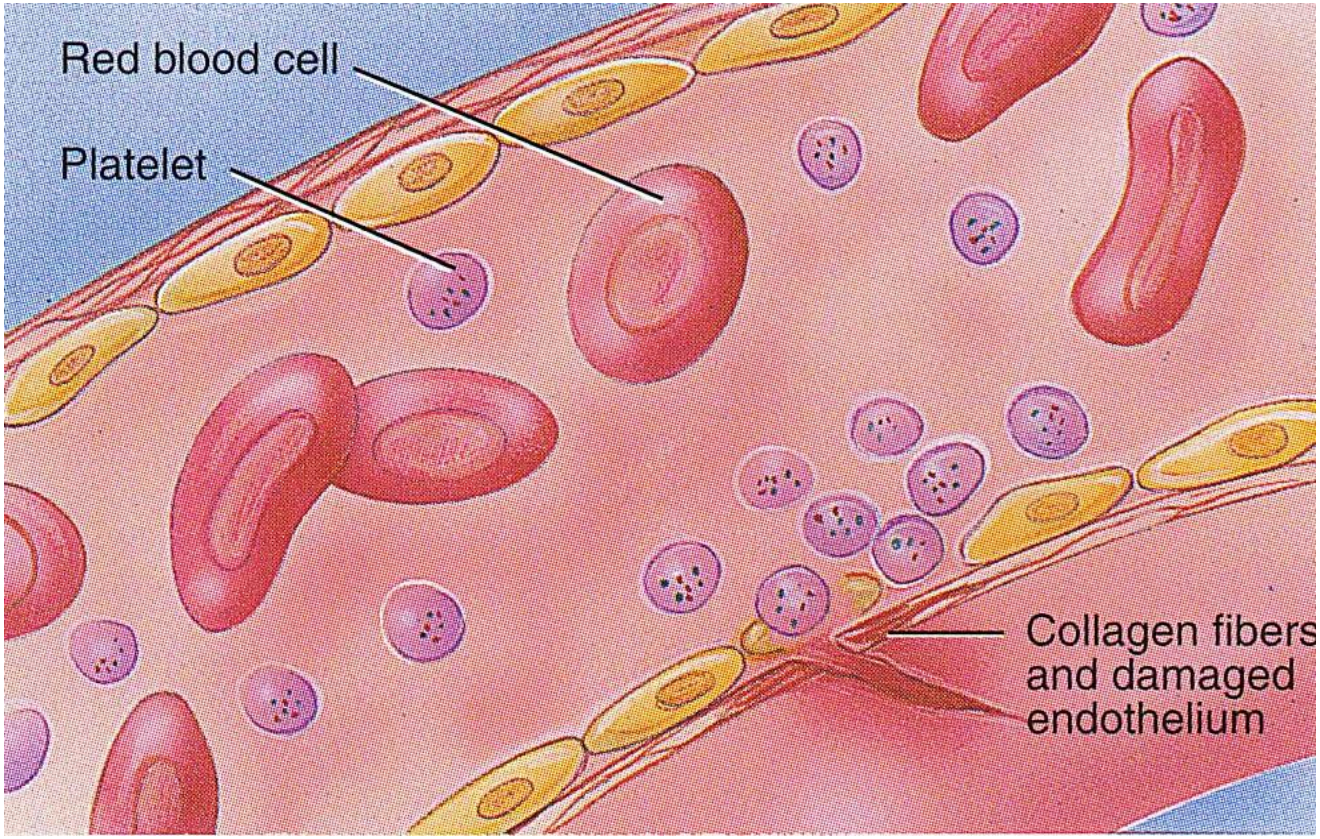
–Adhere to injured site of blood vessel to stop bleeding.
–Secretes substances which are important for clot formation.

Platelet Activation

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

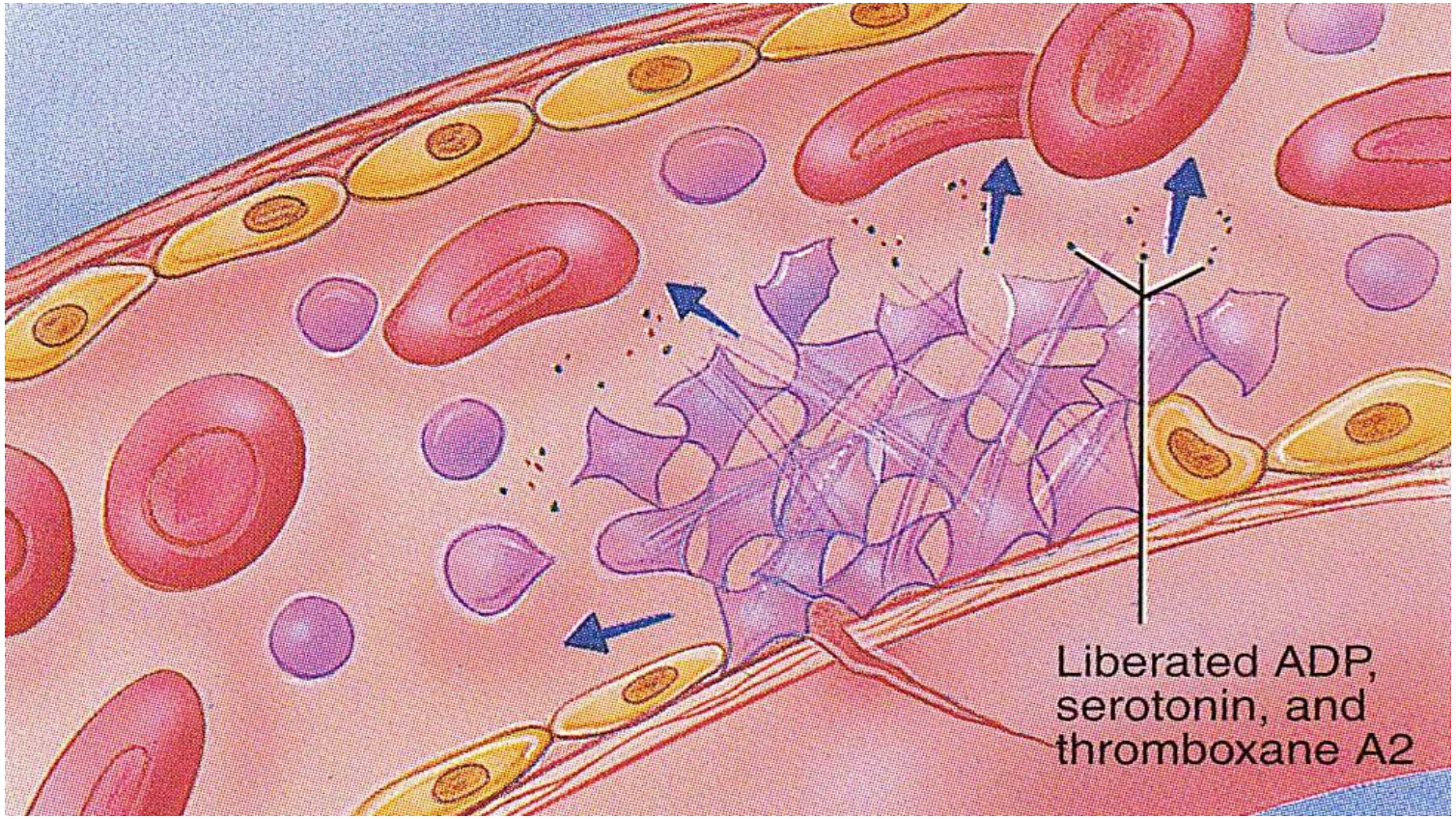
Platelet Adhesion

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



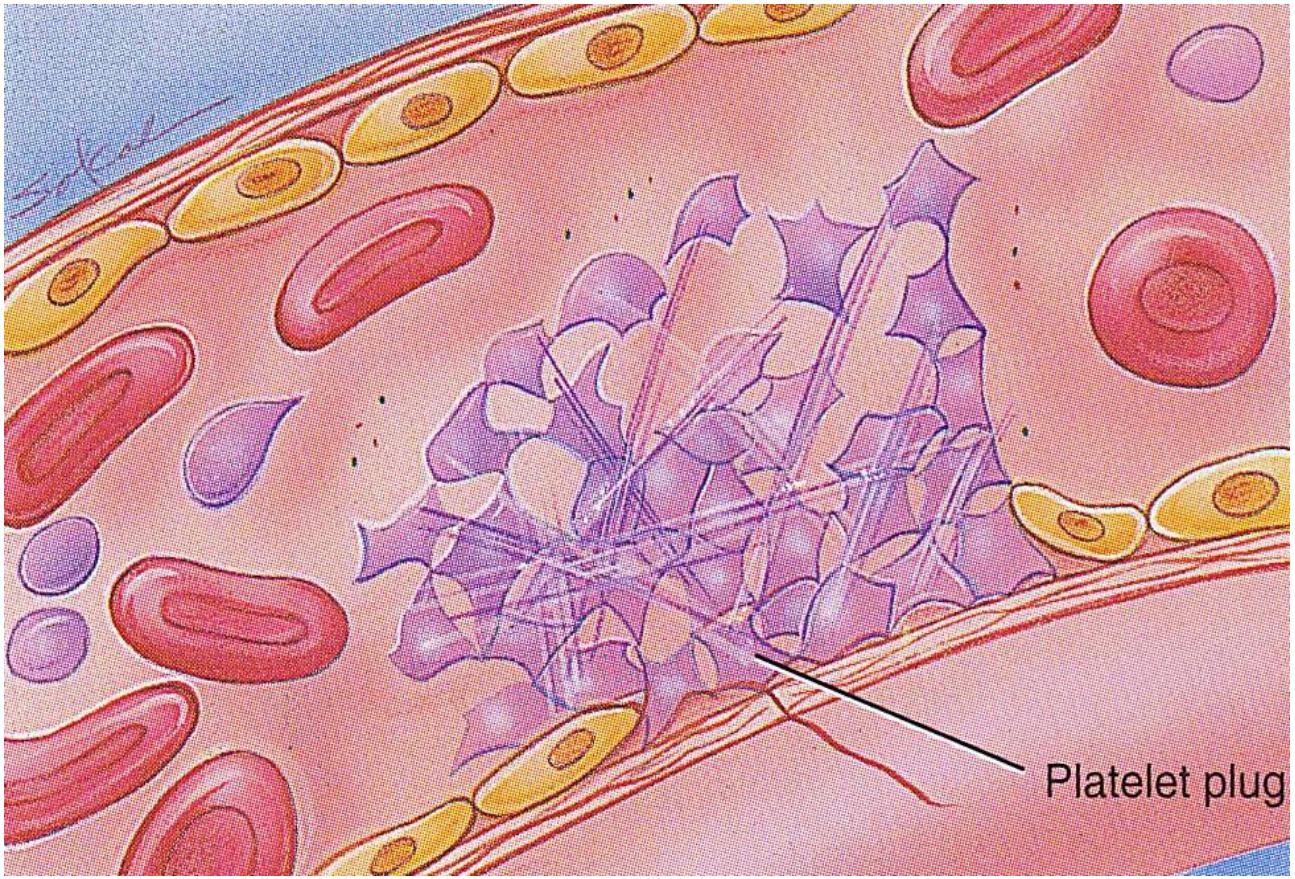
Platelet Release Reaction

- **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 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

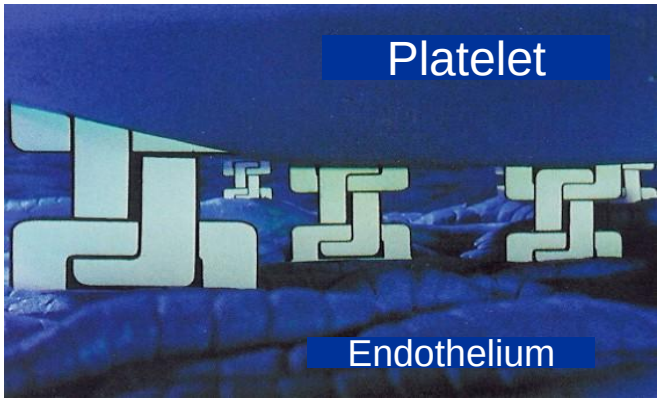


Platelet shape change and Aggregation

Platelet Activation

- Shape change
- Aggregation
- Release
- Clot Retraction

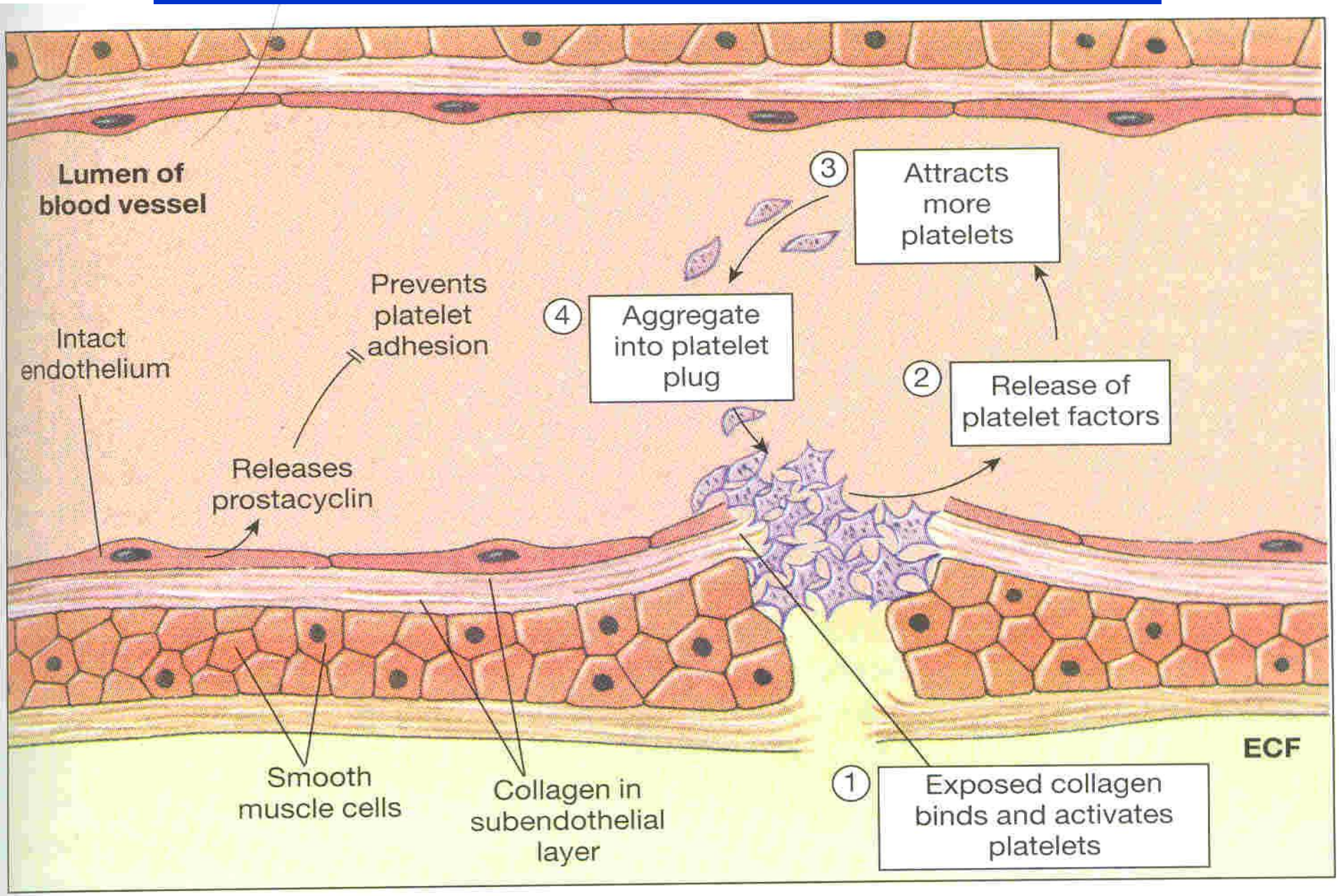
1. Adhesion



2. Shape change

3. Aggregation

Platelet plug formation



Platelet Plug

Aggregation of platelets at the site of injury to stop bleeding

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

- Intact endothelium secret prostacyclin.

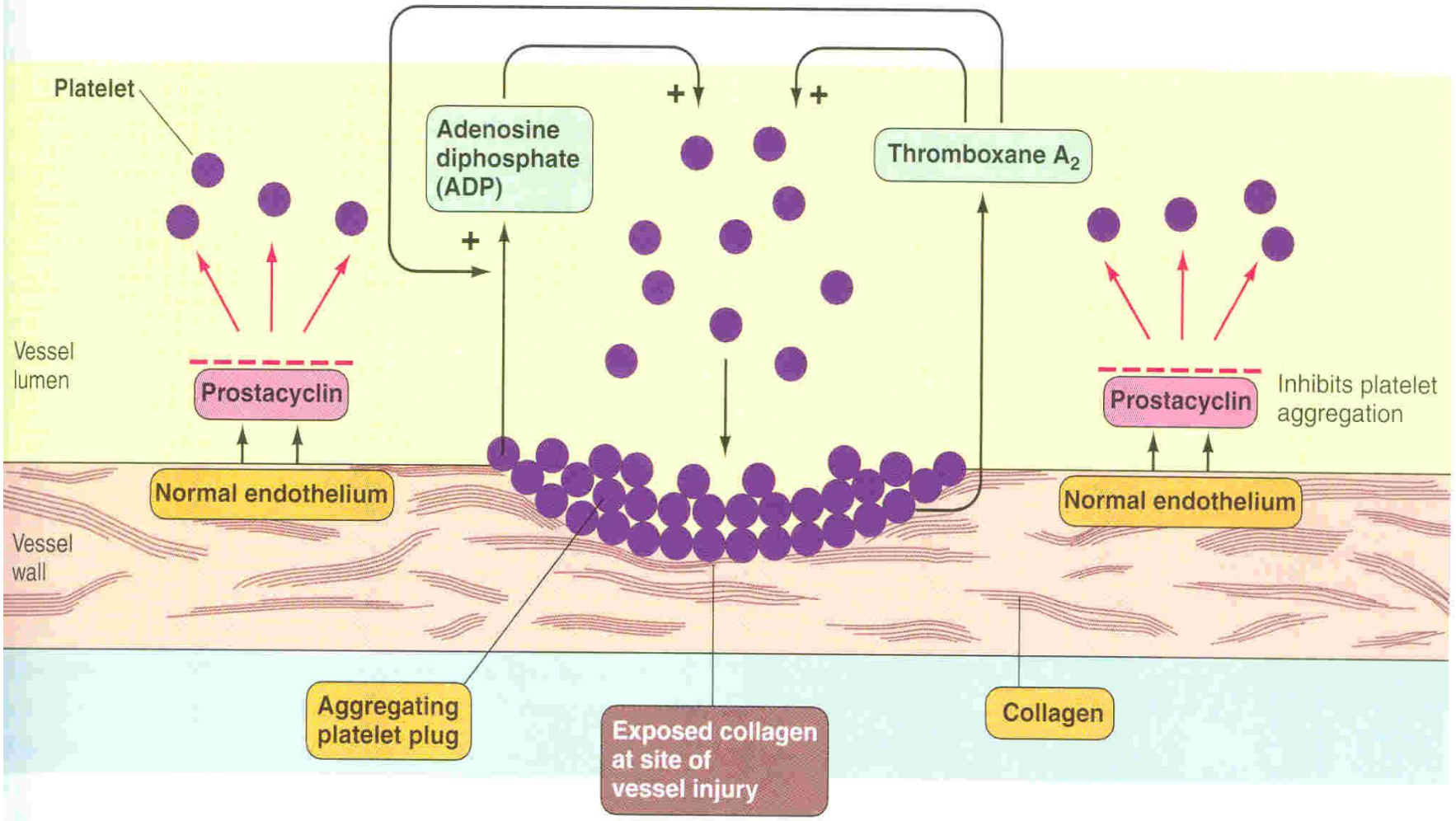
Activated Platelets

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)


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

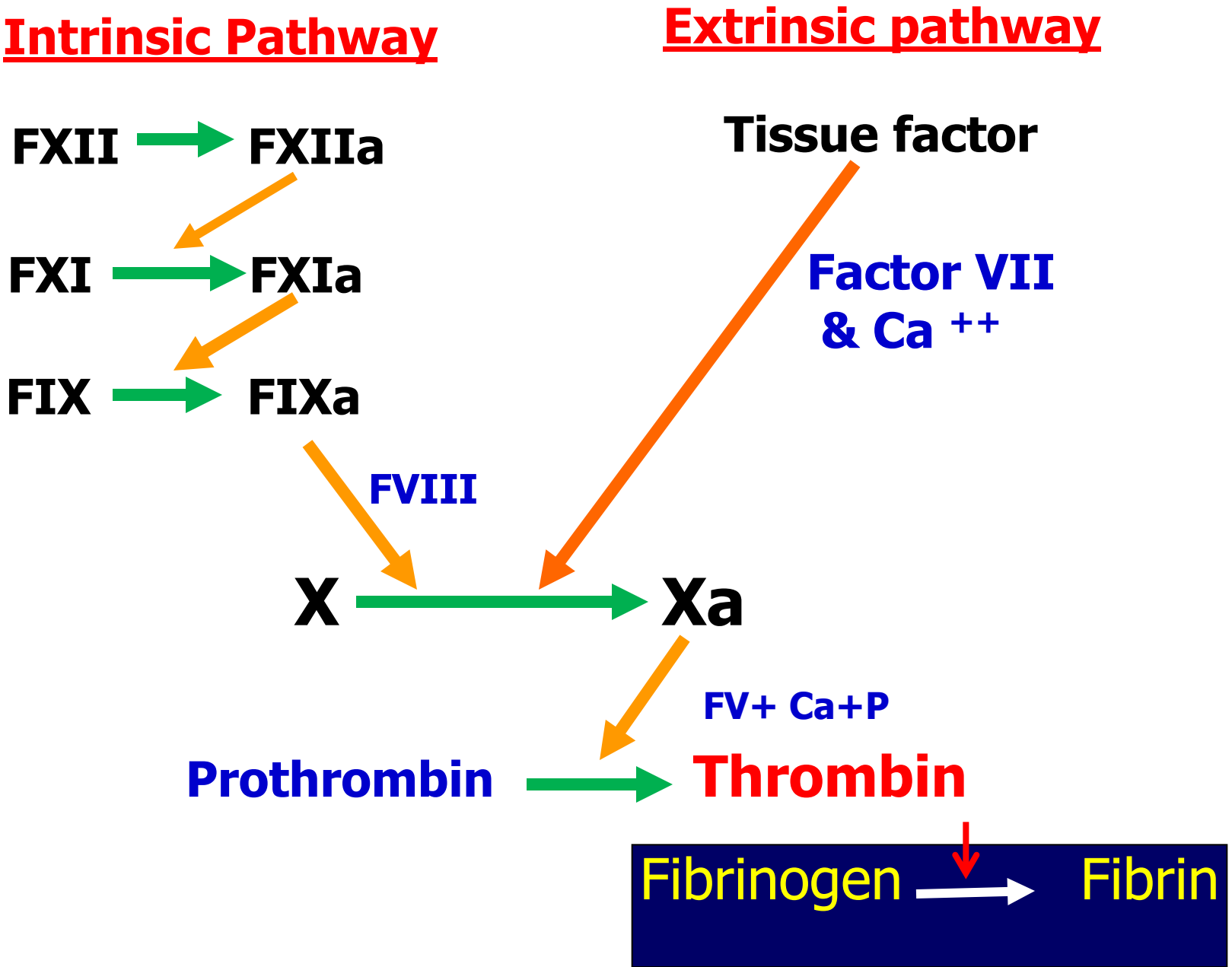
Memostatic Mechanisms:

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

Clotting Factors

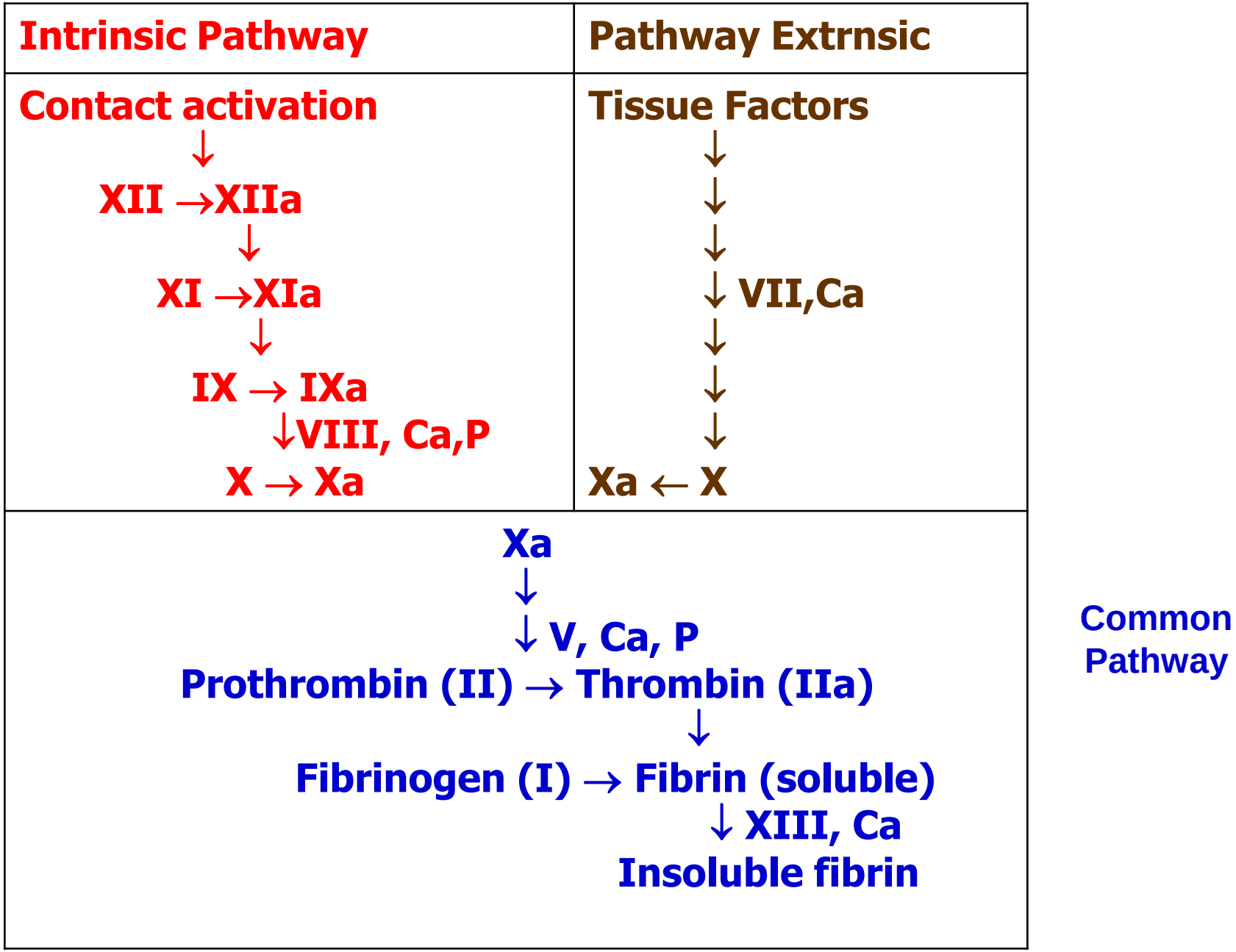
Factors	Names
I	Fibrinogen
II	Prothrombin
III	Thromboplastin
IV	Calcium
V	Labile factor
VII	Stable factor
VIII	Antihemophilic factor
IX	Antihemophilic factor B
X	Stuart-Power factor
XI	Plasma thromboplastin antecedent (PTA)
XII	Hagman factor
XIII	Fibrin stablizing factors

The Coagulation Cascade



Blood coagulation

- 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.


Intrinsic Pathway
Pathway Extrnsic
Contact activation
XII →XIIa
XI →XIa
IX → IXa
↓VIII, Ca,P
X → Xa
Tissue Factors
↓ VII,Ca
Xa ← X
Xa
↓ V, Ca, P
Prothrombin (II) → Thrombin (IIa)
Fibrinogen (I) → Fibrin (soluble)
↓ XIII, Ca
Insoluble fibrin
Common Pathway

Intrinsic pathway (contact 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.
- Xla will activate IX.
- IXa + VIII + platelet phospholipid + Ca activate X.
- Following this step the pathway is common for both.

Extrinsic pathway (Tissue factor pathway)

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

Common pathway:

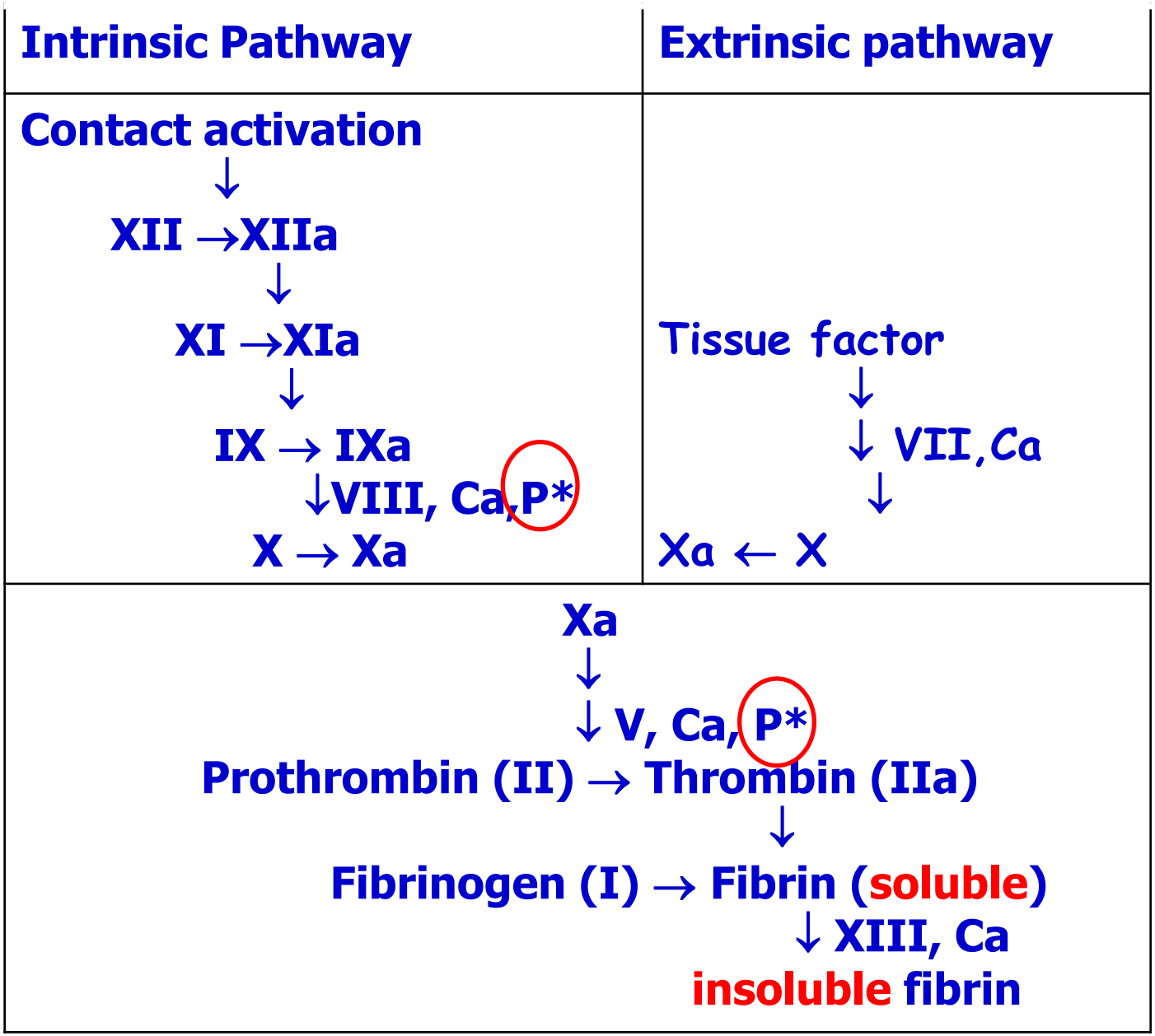
- Xa + V +PF3 + Ca (prothrombin activator) it is a proteolytic enzyme activate prothrombin → thrombin
- Thrombin act on fibrinogen → fibrin monomers (threads)
- Factor XIII + Ca → strong fibrin (strong clot).

Activation Blood Coagulation

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

- **Extrinsic Pathway**: triggered by tissue factor

Common Pathway



P* = phospholipid from platelets

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

Hemostasis:

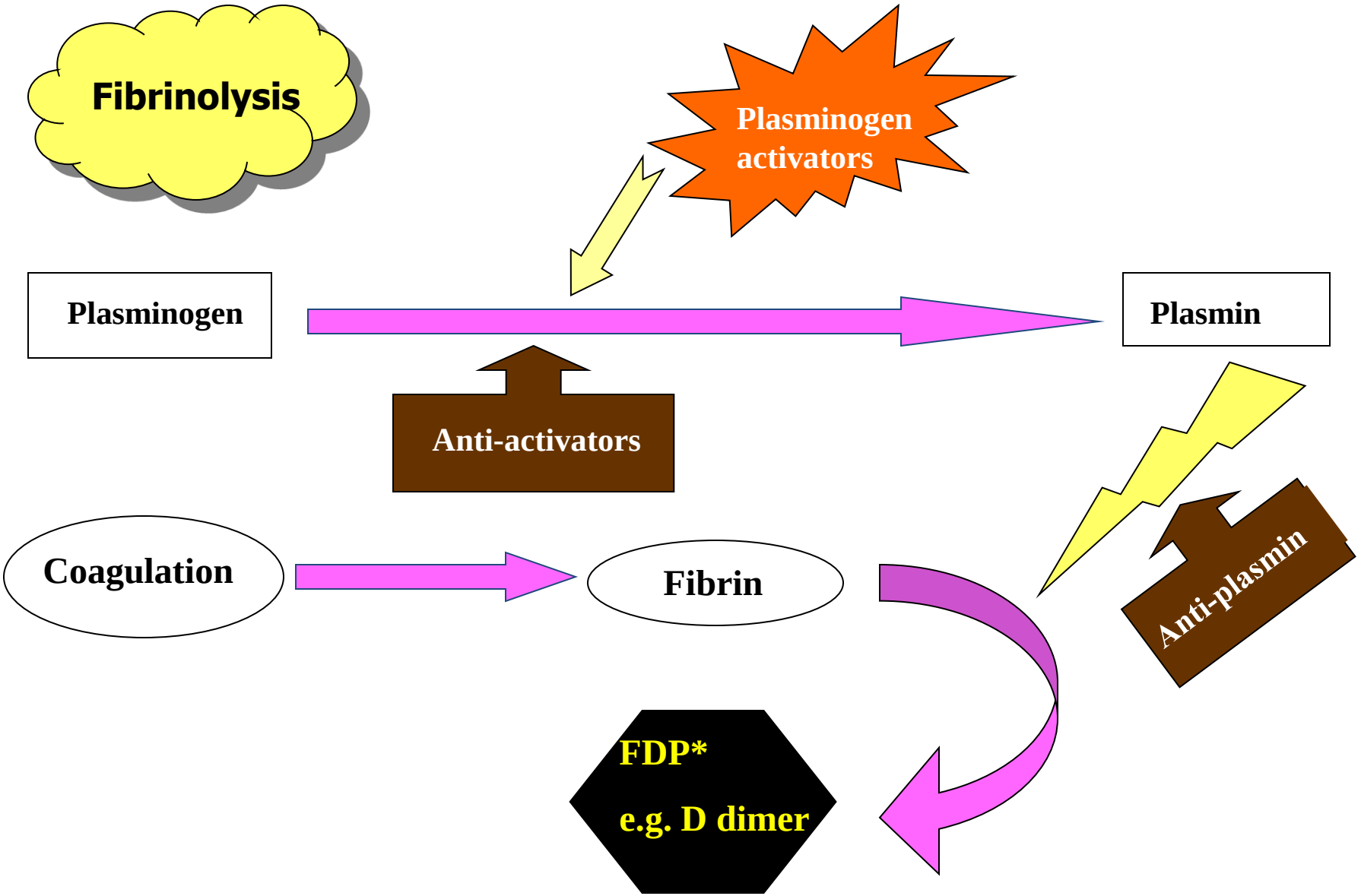
the spontaneous arrest of bleeding from ruptured blood vessels

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

- 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) e.g. D-dimer.
- 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 and cerebral clots.

Objectives

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

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

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

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