PHYSIOLOGY Team 433

Lecture 11:
Haemostasis

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Color Index

Blue = Main Topic
Violet = sup topic
Red = important
Orange = Explanation

White &Black = Addition

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Objectives:

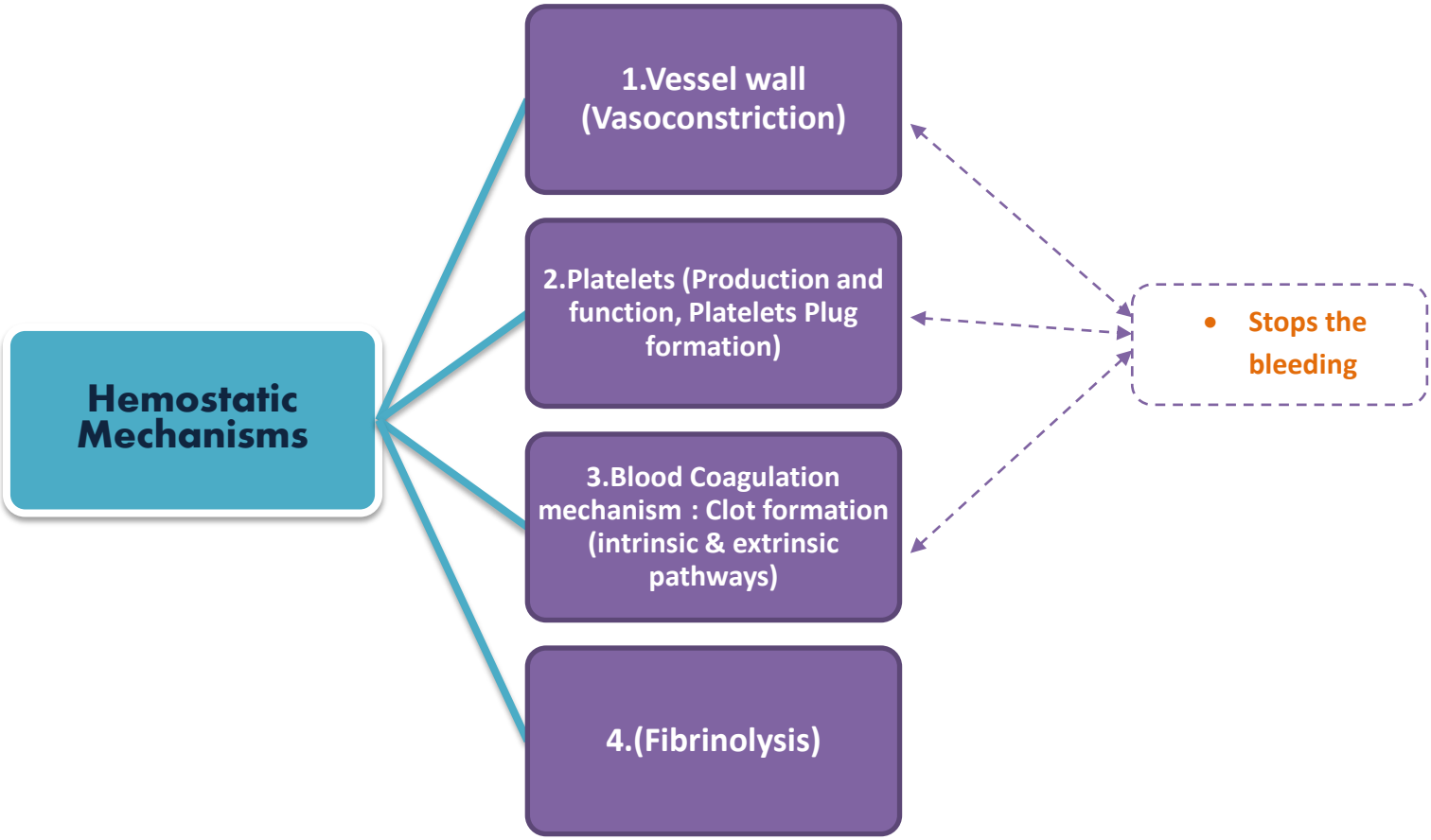
At the end of this lecture you should be able to:

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.
6. Describe the cascade of intrinsic pathway.
7. Describe the cascade of extrinsic and common pathways.
8. Recognize the role of thrombin in coagulation.
9. 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 & extrinsic pathway) and function of thrombin.
6. Fibrinolysis and plasmin.

Haemostasis



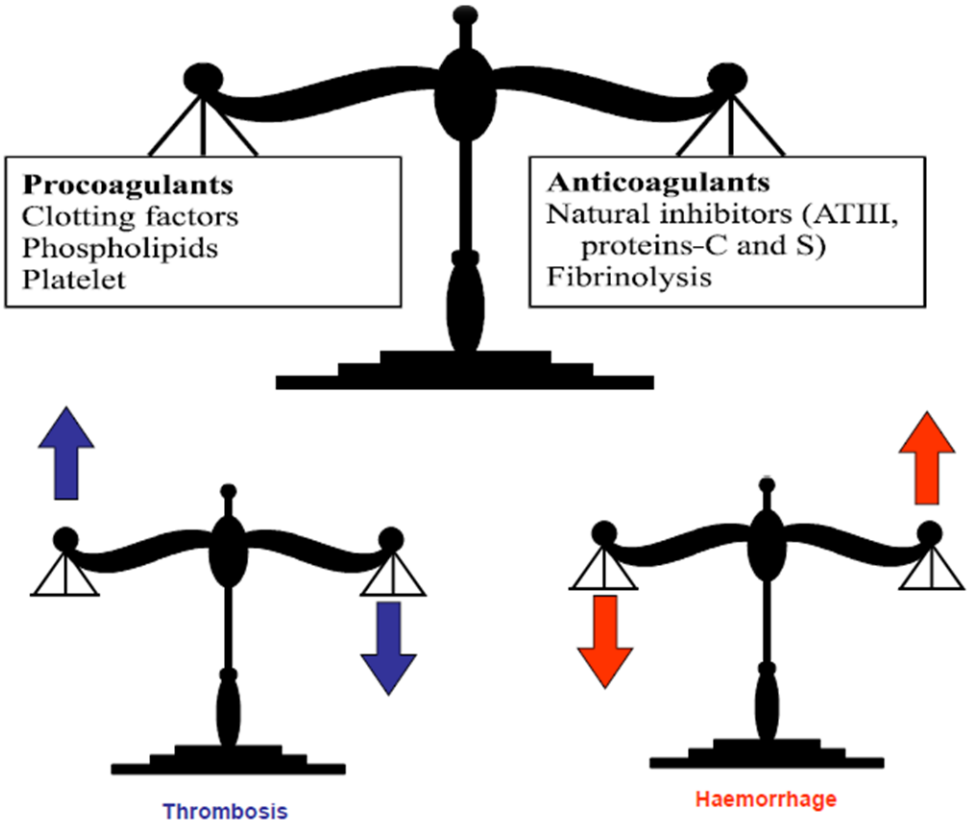
Haemostasis:

The spontaneous arrest of bleeding from ruptured blood vessels.

Homeostasis of the clotting system

• A crucial physiological balance exists between factors favoring clotting (procagulants) and factors that oppose it (anticoagulants).

•Disturbances in this balance can lead to thrombosis or bleeding.



- Procoagulants (تساعد على التجلط او التخثر).
- Anti-coagulants (العكس).
- There is a balance between them.

Mechanisms

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

Heamostatic mechanism:

1. Vessel wall

Immediately After injury a localized Vasoconstriction of smooth muscles

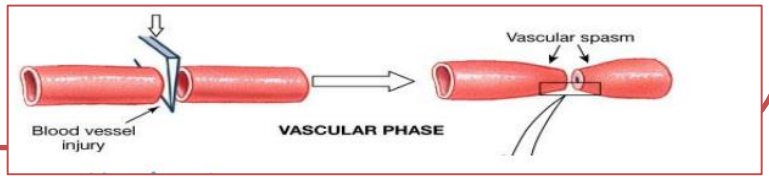
* Contraction of smooth muscles in the vessel wall

Mechanism (Vasoconstriction)

-Hurmoral factors (exists in blood).

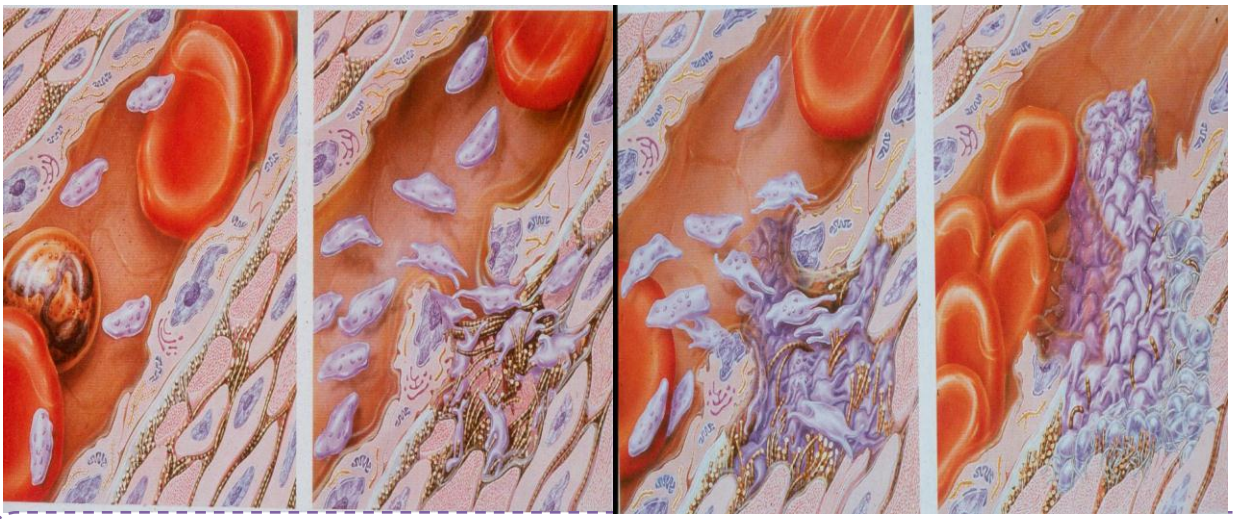
1. local release of thromboxane A2 & 5HT (serotonin) by platelets.
2. Systemic release of adrenaline (by sympathetic NS).

- Nervous factors.



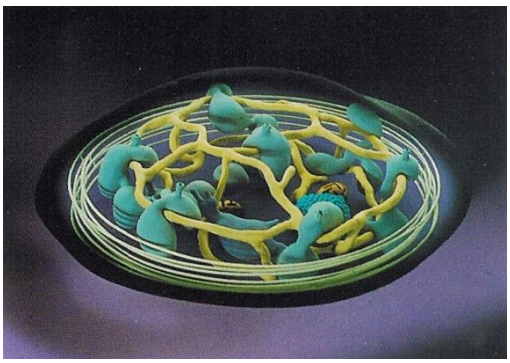
Mechanisms

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

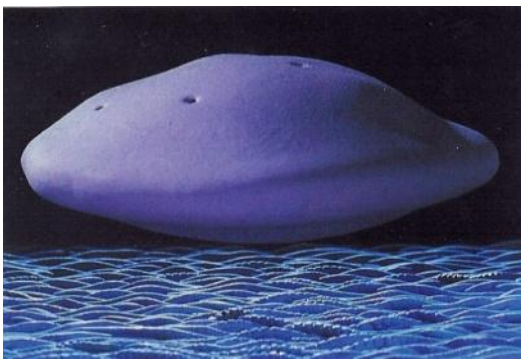


*when the blood is exposed to subendothelial collagen or anything besides smooth endothelium the platelets get activated and they are attracted to aggregate in the site of injury

(Active platelet)



(Inactive platelet)



Platelets_ cont.

Site of formation:

Bone marrow

Steps :

Stem cell

⬇

Megakaryoblast

⬇

Megakaryocyte

⬇

Platelets

- **Note:**

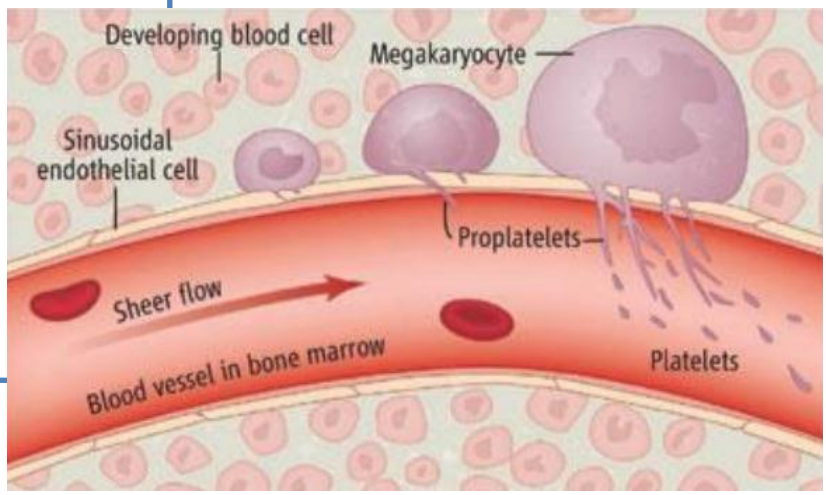
Platelets surface is rich in glycoproteins and phospholipids. (phospholipids has an important role in the clotting system)

Megakaryocytes and platelets formation:

Thrombocytes are:

Fragments of megakaryocytes

in the bone marrow.



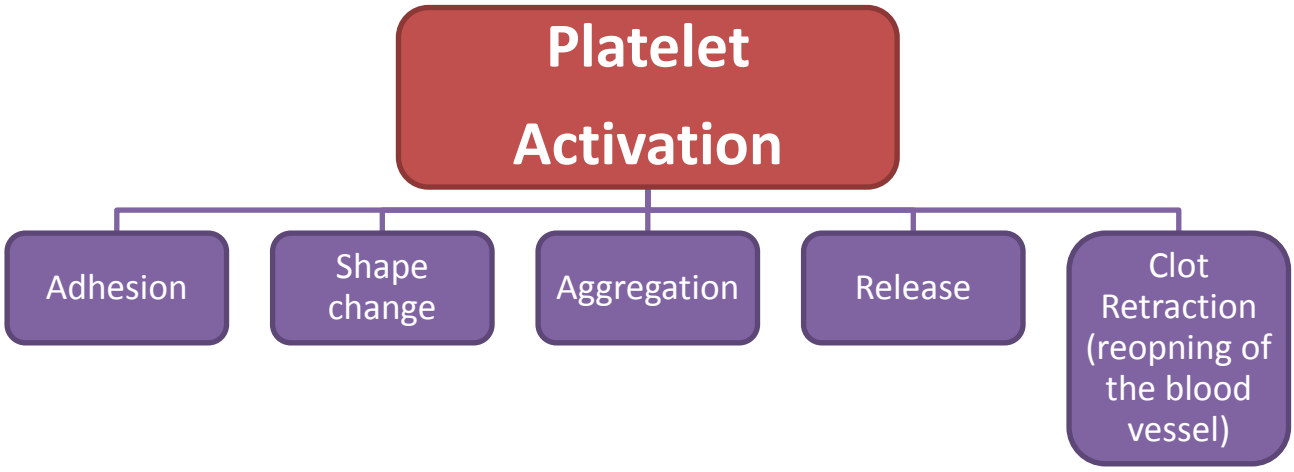
- **Platelet count = 150x103-300x103/ml.**
- **Life span 8-12 days.**
- **Active cells contain contractile protein.**
- **Contain high calcium content & rich in ATP.**

PLATLETS FORMATION (THROMBOIESIS)

- **Regulation of thrombopoiesis By Thrombombopoietin.**

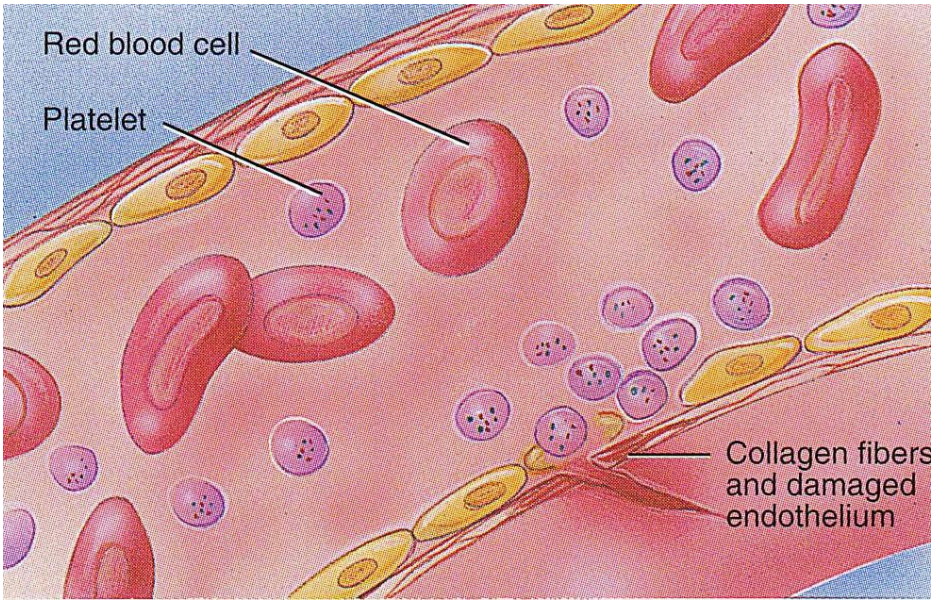
PLATLETS FUNCTION:

- **Begins with platelets activation.**
- **Adhere to injured site of blood vessel to stop bleeding.**
- **Secretes substances which are important for clot formation.**



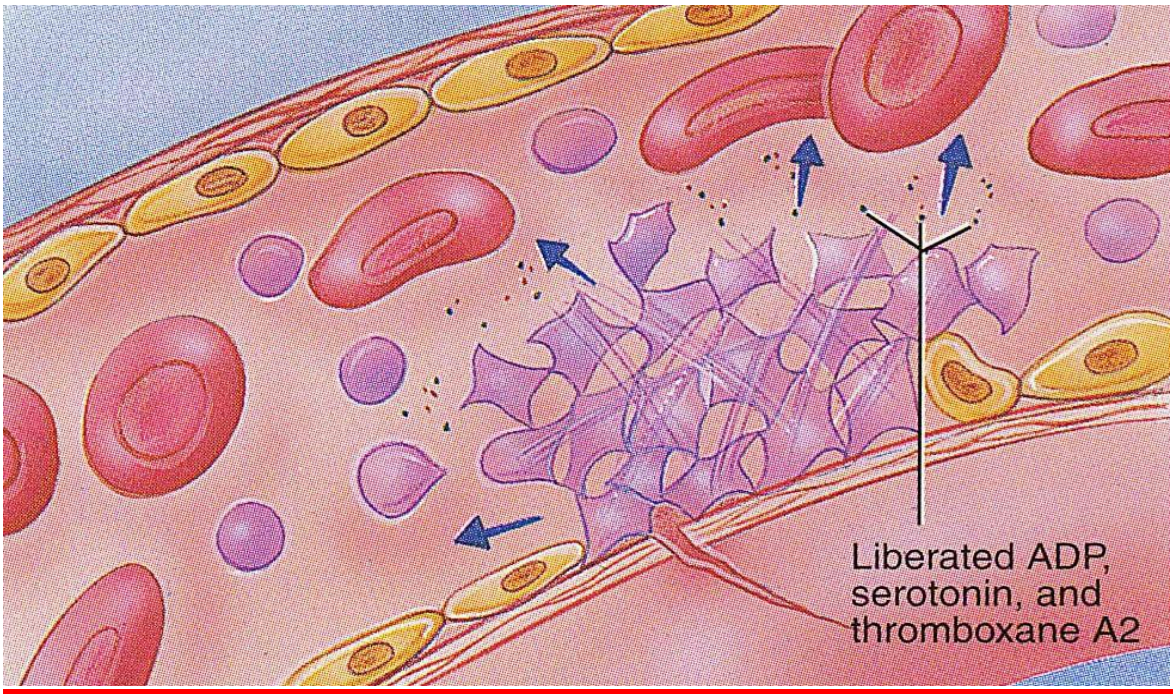
PLATELET ADHESION:

- 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 .



Thromboxane A2:

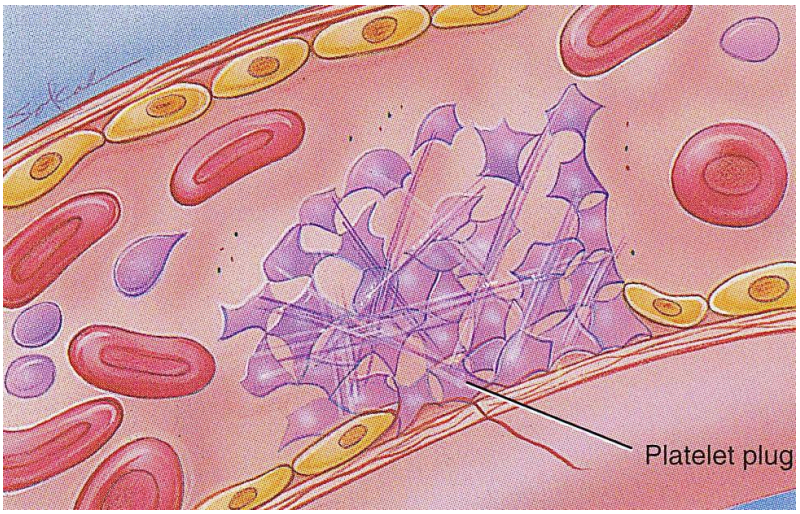
1. Stimulates platelet aggregation.
2. Vasoconstriction.

ADP:

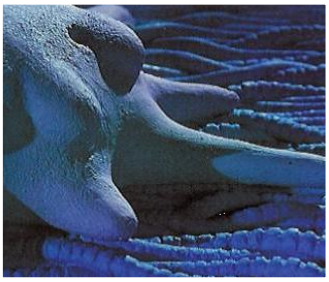
1. Activates other platelets
2. Cause stickiness

PLATELET AGGREGATION :

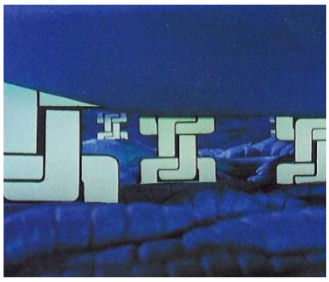
- **Activated platelets stick together and activate new platelets to form a mass called a platelet plug.**
- **Plug reinforced by fibrin threads formed during clotting process .**



2. Shape change



1.Adhesion



3.aggregation

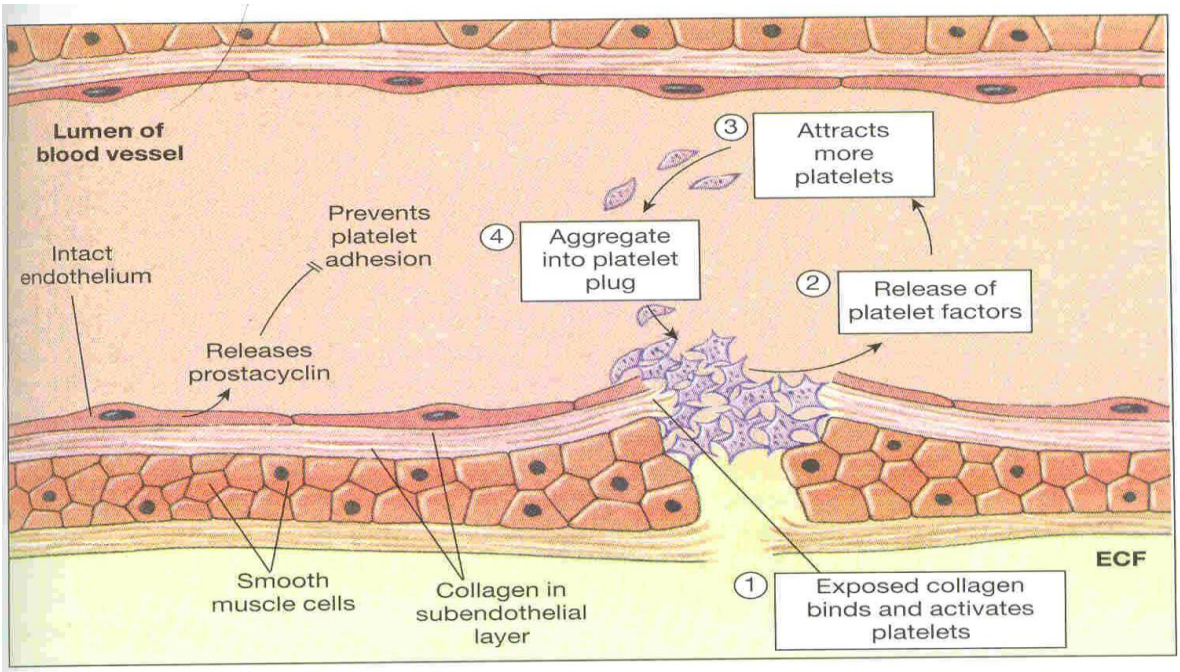
PLATELET PLUG:

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.

*Prostacyclin: produces thromboxane A2



ACTIVATED PLATELETS :

1.5HT→vasoconstriction

2.Platelet phospholipid (PF3)→ clot formation

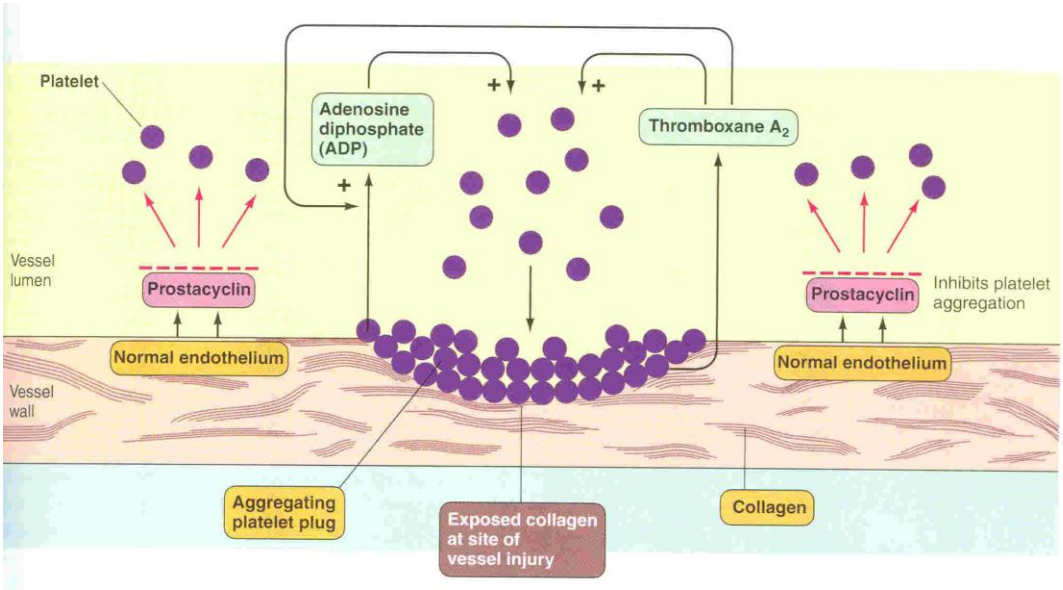
3.Thromboxane A2 (TXA2) is a prostaglandin formed from arachidonic acid

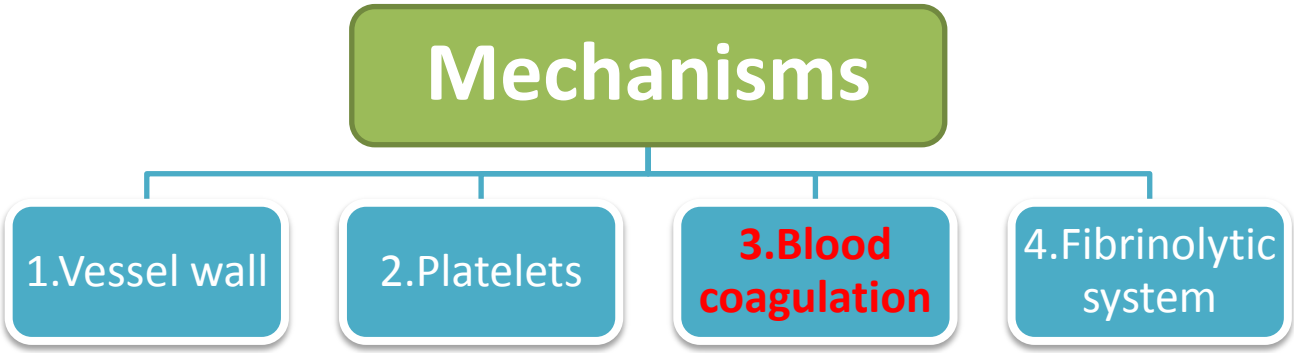
Function:

- **vasoconstriction**
- **Platelet aggregation**

(TXA2 inhibited by aspirin)

- **For people over 40 it is better to take podiatric aspirin.**
- **Aspirin decreases the synthesis of TXA2 = decrease in vasoconstriction and platelets aggregation.**





Clotting Factors:

Factors	Names
I	Fibrinogen (the breaking down of it gives fibrin)
II	Prothrombin (inactive enzyme)
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 (calcium)

The Coagulation Cascade

Intrinsic Pathway (contact pathway)

- All factors are presence in blood

FXII 12 (contact factor) → FXIIa (active)

FXI 11 → FXIa

FIX 9 → FIXa

FVIII 8

Extrinsic pathway: (fast pathway)

Tissue factor (tissue thromboplastin)

- Inside the tissue

Factor VII 7 & Ca ++

X → Xa (common pathway)

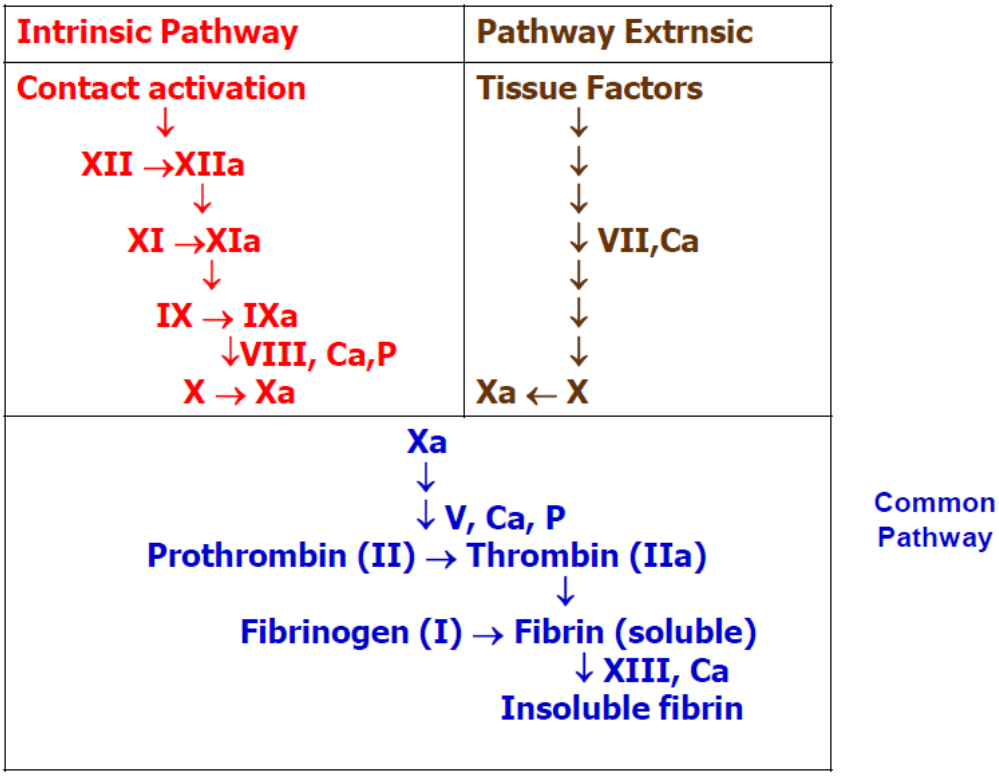
FV 5 + Ca+ P (phospholipid)

Prothrombin → Thrombin

Fibrinogen → Fibrin

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 (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.**
- **XIa 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:

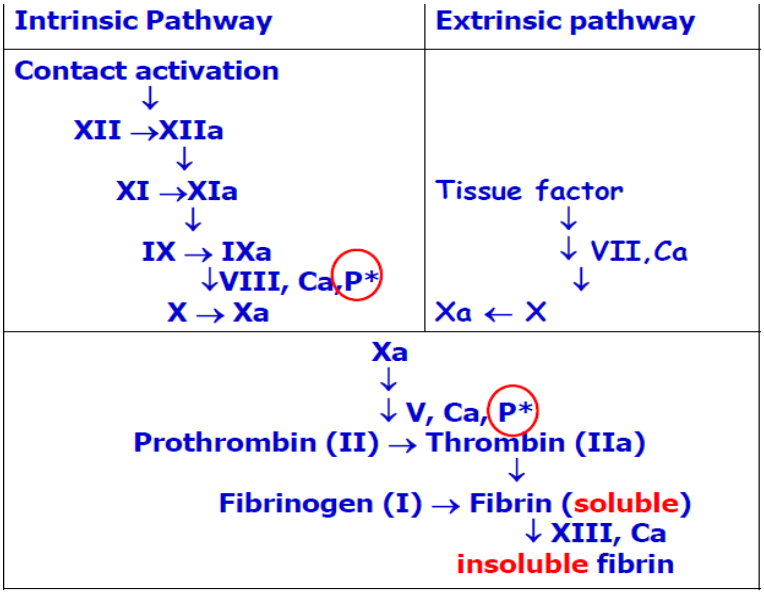
- **Intrinsic Pathway:**

All clotting factors present in the blood

- **Extrinsic Pathway:**

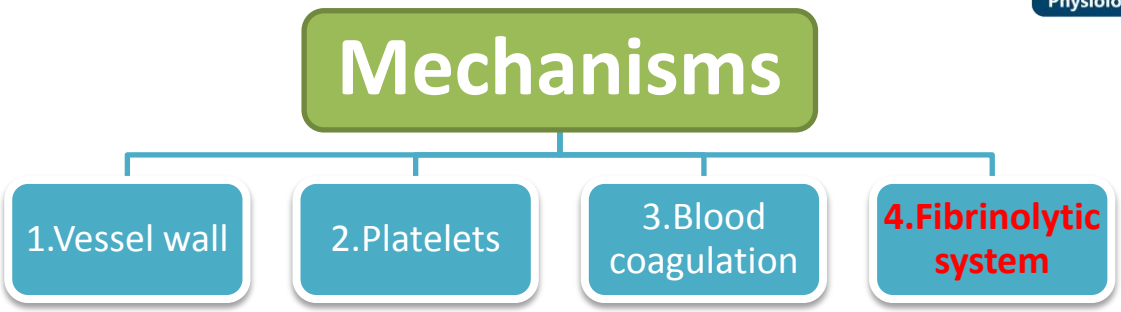
Triggered by tissue factor

- **Common Pathway**



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 :

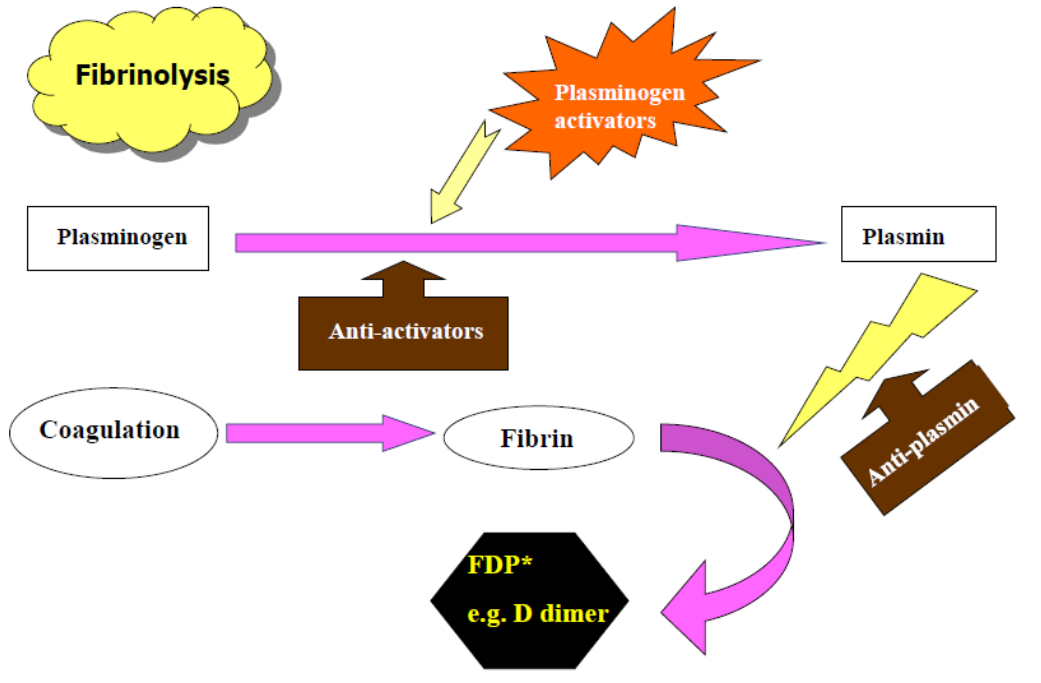
•Formed blood clot can either become fibrous or dissolve.

•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 inhibitors and activators keep it under control.

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 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.

Summary:

- **Haemostasis mechanisms include :**
  (Vessel wall – Platelets – Blood clotting – Fibrolysis)
- Disturbances between procougalnt and anticogulant can lead to thrombosis or bleeding.
- **Regulation of thrombopoiesis By Thrombombopoietin**
- **Platelets Activation include :**
  (Adhesion – Change shape – Aggregation – Relase – Clot retraction)
- **Thrombin will change fibrinogen (plasma protein) to fibrin (insoluble protein).**
- **Fibrinolysis (dissolving) = Break down of fibrin by naturally occurring enzyme plasmin therefore prevent intravascular blocking**
- **Plasmin is present in the blood in inactive form plasminogen.**

Related videos:

1. https://www.youtube.com/watch?v=f9Ojq9f2qaM (clots, thrombi & antiplatelets)
2. https://www.youtube.com/watch?v=s4FoSf6Yi_s&feature=c4-overview-vl&list=PLzl4lgX_3Rvczcmakc5EaSeE5Tqbu3w7k (coagulation cascade)
3. https://www.youtube.com/watch?v=ys8fMaqfq4Q&list=PLzl4lgX_3Rvczcmakc5EaSeE5Tqbu3w7k (anticoagulation& thrombolytics)

Multiple Choice Questions

Q1: Thrombopoietin is hormone that raised from?

A- Spleen
B- Bone marrow
C- Lymph nodes
D- Liver

Q2: Prevention of blood loss is a definition of?

A- Homeostasis
B- Hemostasis
C- Plasmin
D- Thrombin

Q3: The stickness of platelets is the function of?

A- Thromboxane A
B- D-ADP
C- Serotonin
D- Thrombin

Q4: TXA2 can be inhibited by?

A- Panadol
B- Penicillin
C- Aspirin
D- Morphine

Q5: Which of the following triggered intrinsic pathway?

A- Factor V
B- Factor XIII
C- Factor XII
D- Thromboplastin

Q6: Which of the following will change fibrogen into fibrin?

A- Thrombin
B- Plasmin
C- Factor X
D- Prothrombin

1-D 2-B 3-B 4-C 5-C 6-A