



Physiology
team



13

Hemostasis



Physiology
team

Objectives



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

Describe the formation and development of platelets

Recognize different mechanisms of hemostasis

Describe the role of platelets in hemostasis.

Recognize different clotting factors

Describe the cascades of intrinsic and extrinsic pathways for clotting.

Recognize process of fibrinolysis and function of plasmin.

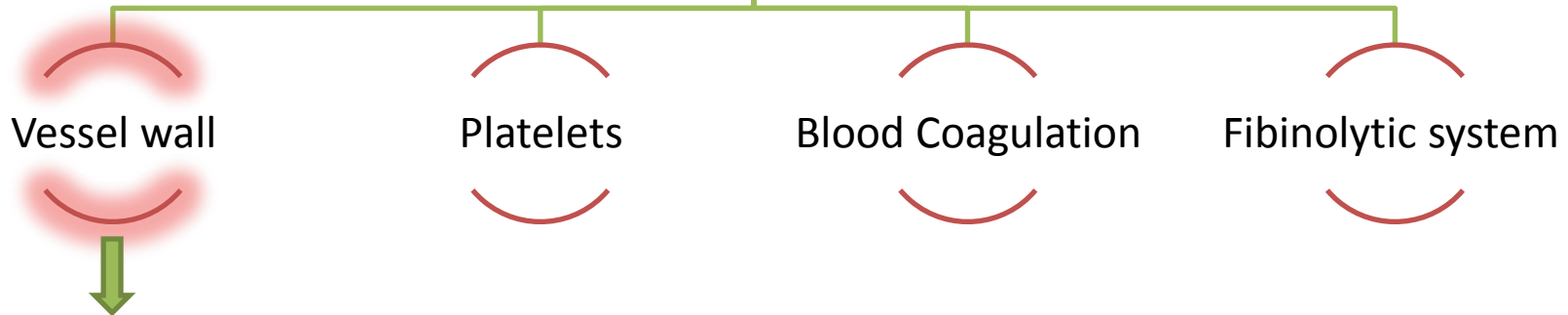


Hemostasis



Hemostasis: the spontaneous arrest of bleeding from ruptured blood vessels.

Hemostasis mechanisms



Vessel wall:

Immediately after injury a localized vasoconstriction of smooth muscles.

Its function is to decrease blood flow through the injured vessel.

mechanism of vasoconstriction:

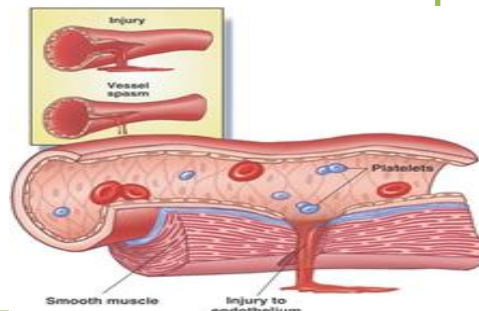
by humoral factors :

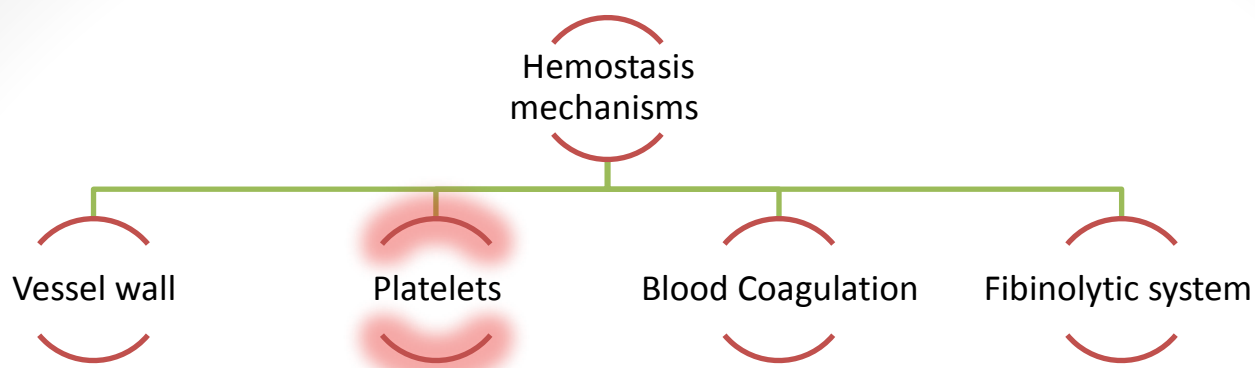
-Adrenaline

-nervous factors

-thromboxane A₂

-serotonin (5HT) by platelets



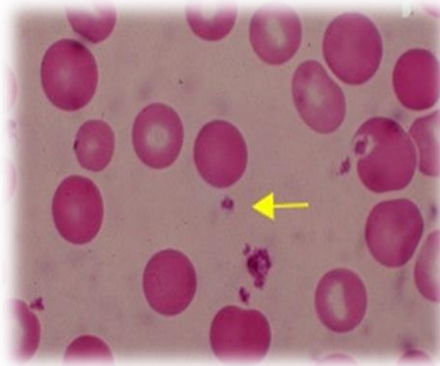


Platelets (PLT):

- small disc shaped Cells
- Platelet count = $150 \times 10^3 - 300 \times 10^3 / \text{ml}$
- life span 8-12 days
- Dense granules Contain:

high calcium content
rich in ADP
serotonin

Active cells contain:
contractile proteins , Fibrinogen, vWF, other proteins.



Platelets formation (Thrombopoiesis):

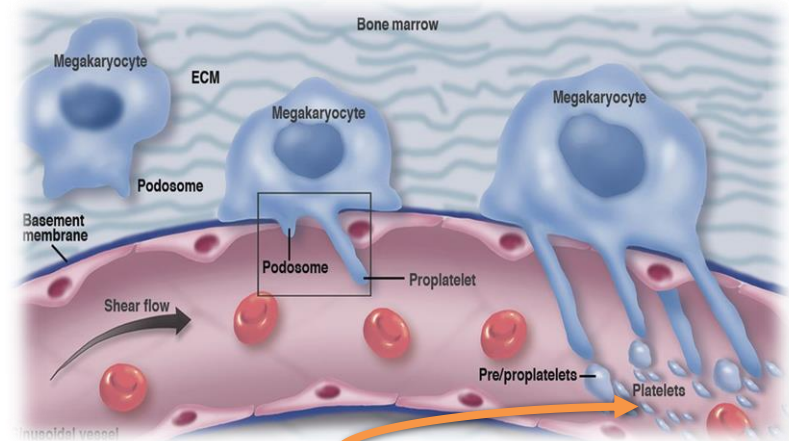
Thrombocytes are Fragments of megakaryocytes.

Site of formation: bone marrow.

Steps of formation:

Stem cell → megakaryoblast → Megakaryocytes → platelets.

Regulation of thrombopoiesis By: Thrombopoietin.



Platelet Function

Begins with **Platelet activation**:

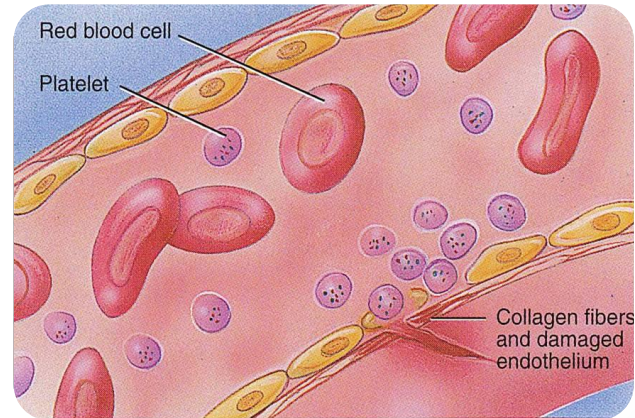
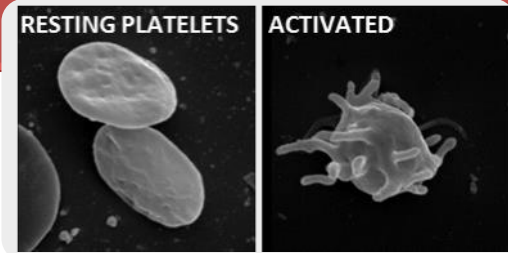
Note
هذه الخطوات تختلف من صفيحة دموية
لأخرى ، يعني أنه غير ضروري أن جميع
الصفائح الدموية تمشي على الخطوات بنفس
الترتيب.



Adhesion:

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

• Platelets are activated by adhesion
• Extend projections to make contact with each other

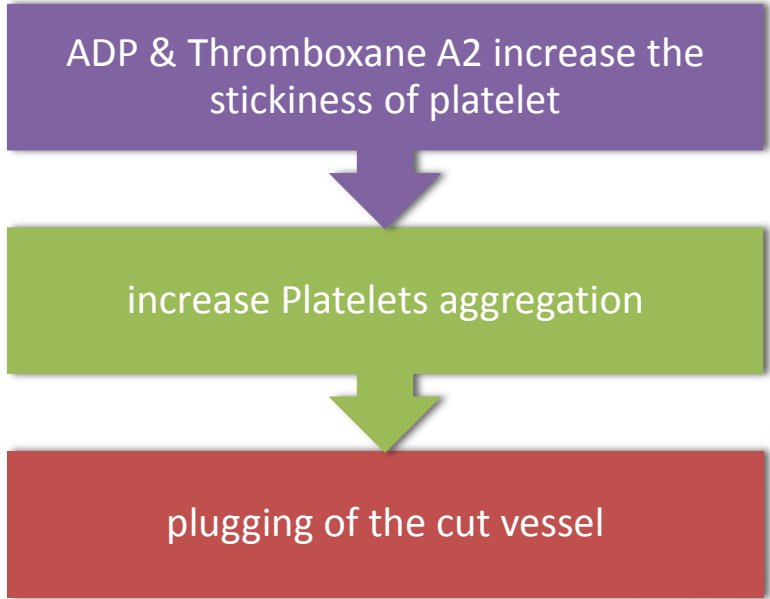
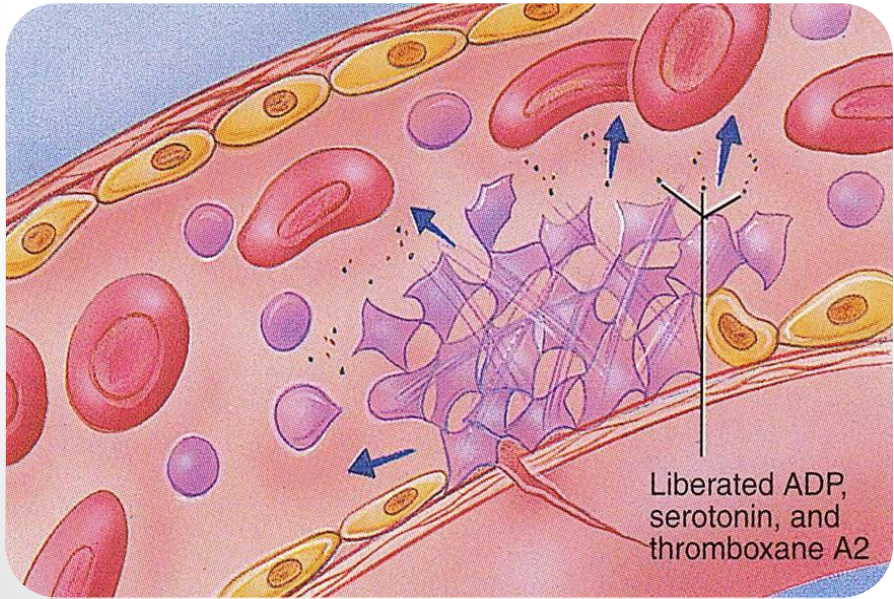


Platelet Release Reaction:

Secretions of Activated Platelet

Serotonin (5HT)	vasoconstrictors
Thromboxane A2 (THA2)	- Platelets aggregation. - vasoconstrictors
Platelet phospholipid (PF3)	Clot formation
ADP	- Stimulates other platelets which are in resting state to secrete the substance in it's granules - Cause sticiness

(TXA2) is a prostaglandin formed from arachidonic acid & its inhibited by aspirin

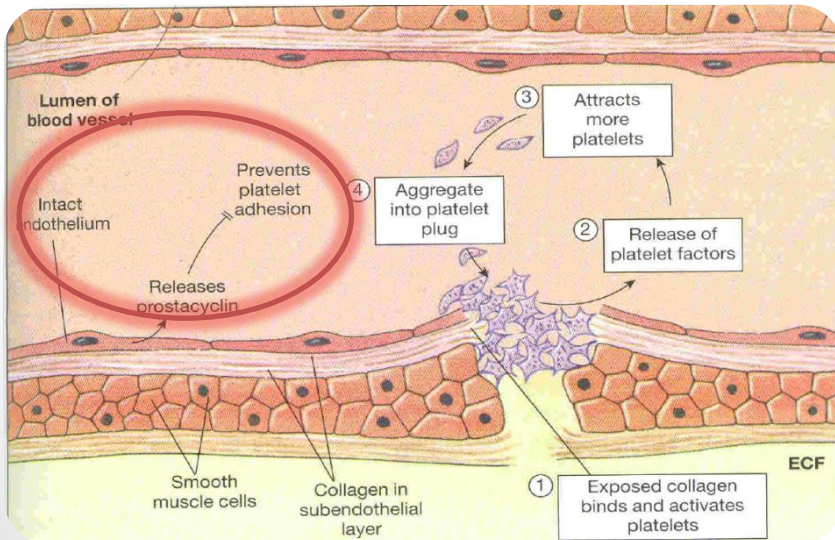


Platelet Aggregation

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

Clot Retraction

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

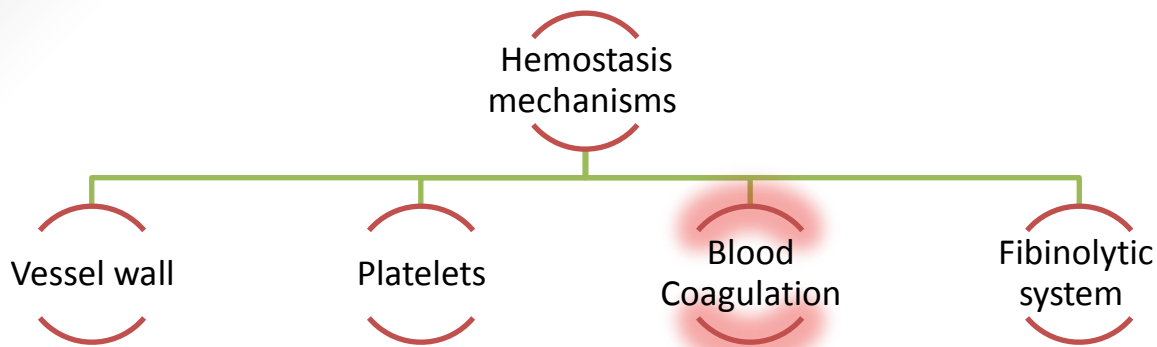


Intact endothelium secret **prostacyclin** and **NO** which inhibit aggregation.

YouTube

[Platelet activation](http://www.youtube.com/watch?v=0pnp0Ey0eYE)

<http://www.youtube.com/watch?v=0pnp0Ey0eYE>



Blood Coagulation

❖ Clotting Factors:

Circulate in plasma in **inactive** state.

Factors	Names
(1) I	Fibrinogen
(2) II	Prothrombin
(3) III	Thromboplastin
(4) IV	Calcium
(5) V	Labile factor
(7) VII	Stable factor
(8) VIII	Antihemophilic factor A
(9) IX	Antihemophilic factor B
(10) X	Stuart-Power factor
(11) XI	Plasma thromboplastin antecedent (PTA)
(12) XII	Hagman factor
(13) XIII	Fibrin stabilizing factors

Memorize only what is colored in red.



Blood coagulation

http://www.youtube.com/watch?v=cy3a_OOa2M

Blood coagulation (clot formation)

A series of **biochemical reactions**
leading to the formation of a blood clot



Activation of **thrombin** enzyme from **inactive** form
prothrombin



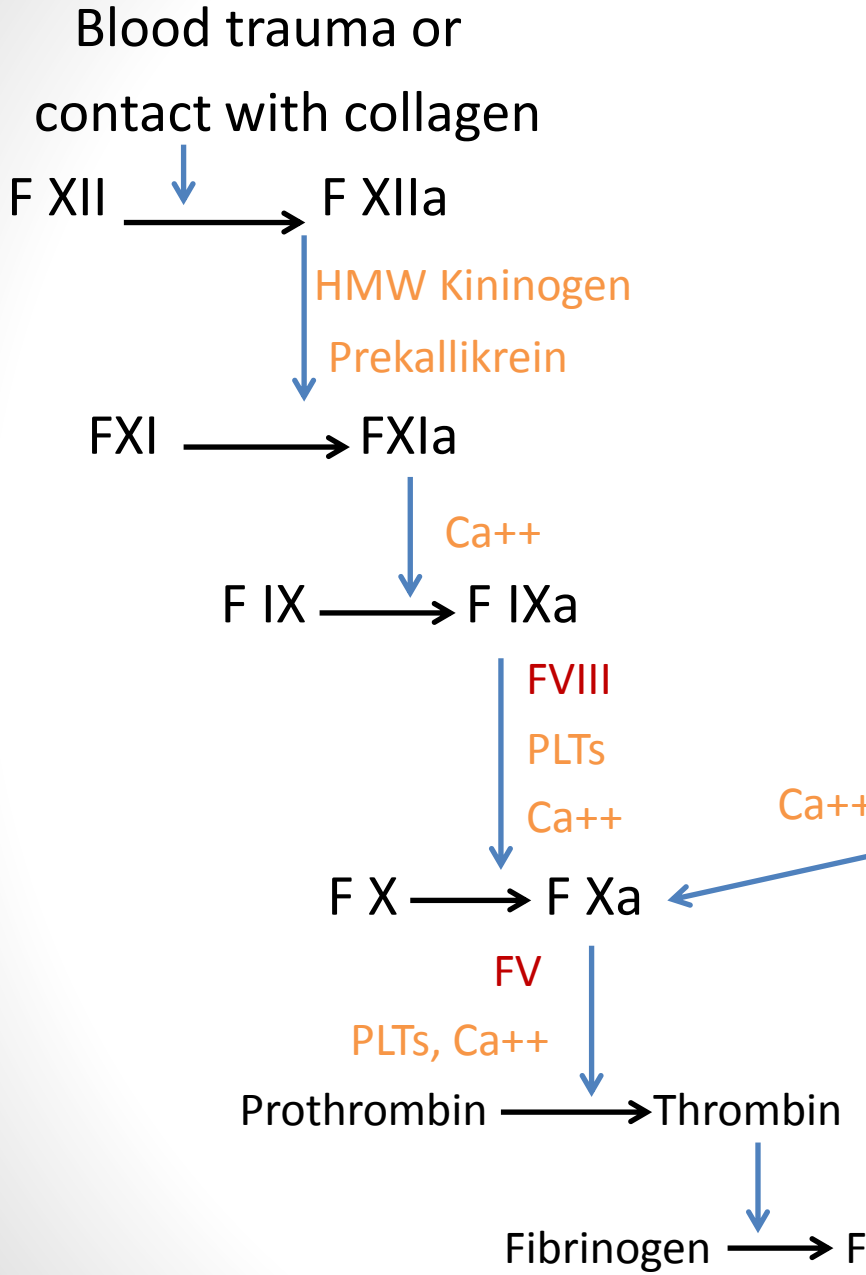
Fibrinogen (plasma protein)
to **fibrin** (insoluble protein)



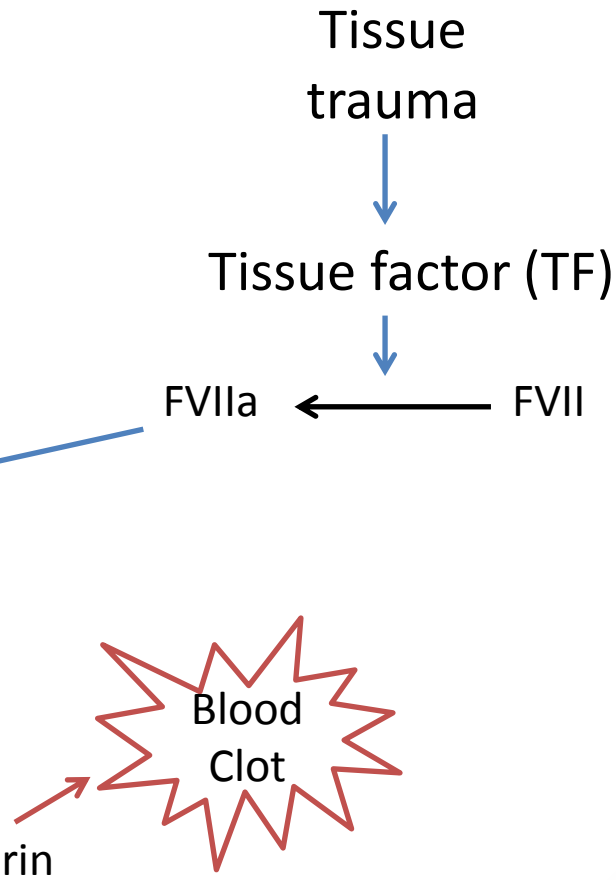
Prothrombin (inactive thrombin) by
a **long intrinsic** or **short extrinsic** pathways

The Intrinsic Pathway

F → Factor
 A → Active
 PLTS → Platelets

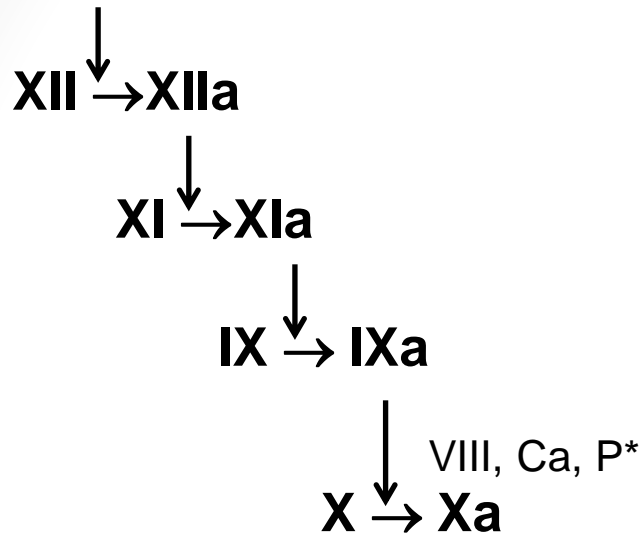


The Extrinsic Pathway



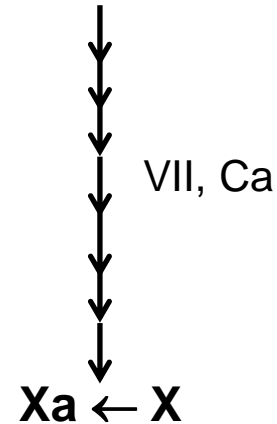
Intrinsic Pathway

Contact activation



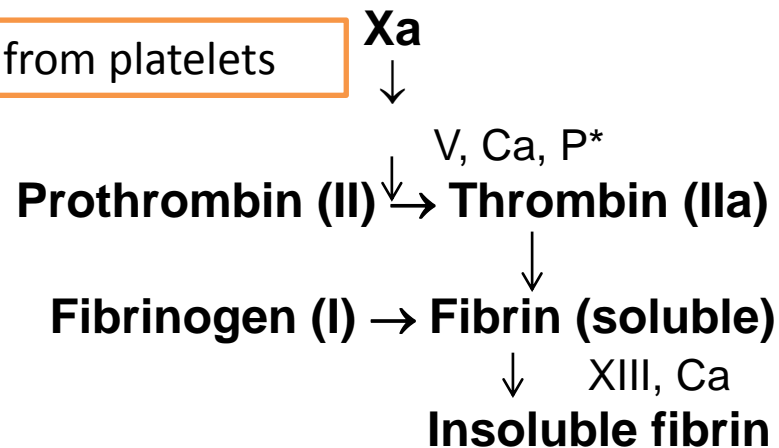
Extrinsic Pathway

Tissue Factors



Common Pathway

P* = phospholipids from platelets



Activation Blood Coagulation

Intrinsic pathway



- The trigger is the activation of factor XII by contact with foreign surface, injured blood vessel, and glass.
- All clotting factors present in the blood.
- Activate factor (XIIa) will activate XI
- XIa will activate IX
- IXa + VIII + platelet phospholipid + Ca activate X

Extrinsic pathway

- Triggered by material released from damaged tissues (tissue thromboplastin).
- Triggered by tissue factor.
- Tissue thromboplastin + VII + Ca \longrightarrow activate X

Common pathway

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

Clotting factors – intrinsic & extrinsic pathways

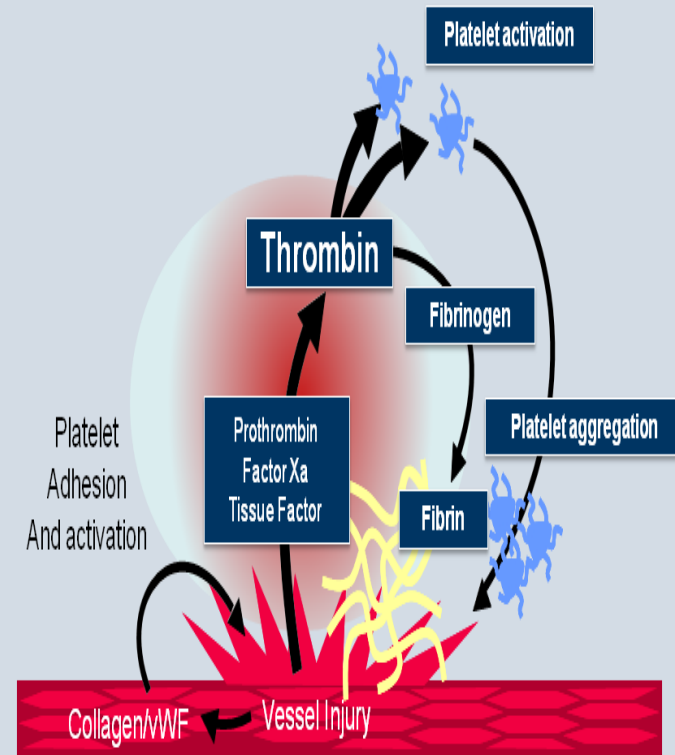
<http://www.youtube.com/watch?v=MPGe-guZMqM>

Thrombin

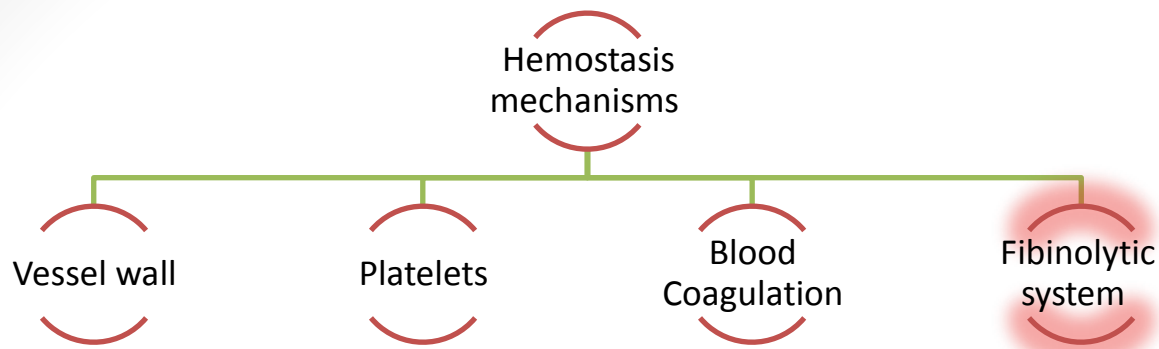
- Thrombin changes **fibrinogen to fibrin**.
- Activates **factor V**
- Thrombin is essential in platelet morphological changes to form **primary plug**.
- Thrombin stimulates platelets to release **ADP & thromboxane A2**; both stimulate further platelets aggregation.

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.



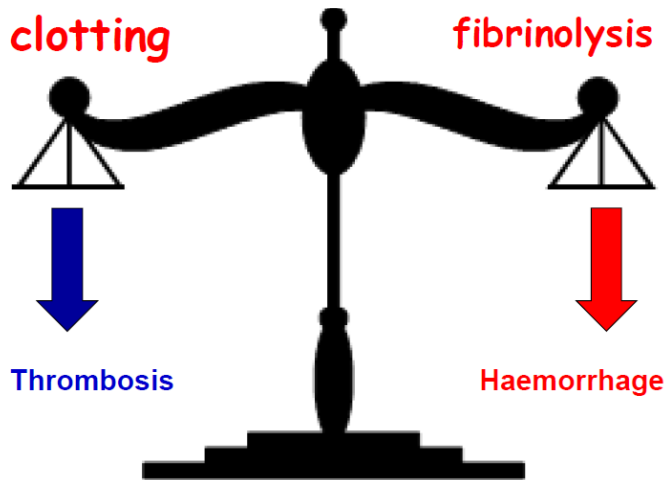
Fibrinolysis:

Fibrinolysis (dissolving) = Break down of fibrin by plasmin enzyme.

There is balance between clotting and fibrinolysis.

Excess fibrinolysis leads to tendency for bleeding (عرضة لحدوث نزيف).

Excess clotting leads to Blocking of blood vessels.



Fibrinolysis

<http://www.youtube.com/watch?v=Y1iQRHw6QoA>

❖ Plasmin:

Plasmin is present in the blood in inactive form (plasminogen)

It is activated by tissue plasminogen activators (t-PA) in blood.

Plasmin converts the fibrin into fibrin degradation products (FDP).

Unwanted effect of plasmin is the digestion of clotting factors.

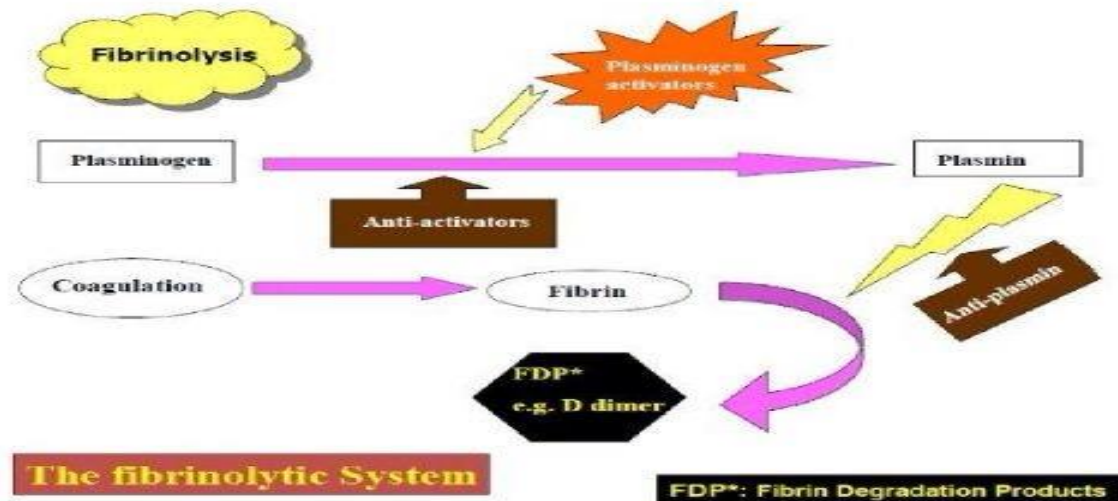
Plasmin is controlled by :

PAI)) Plasminogen Activator Inhibitor

Antiplasmin from the liver.

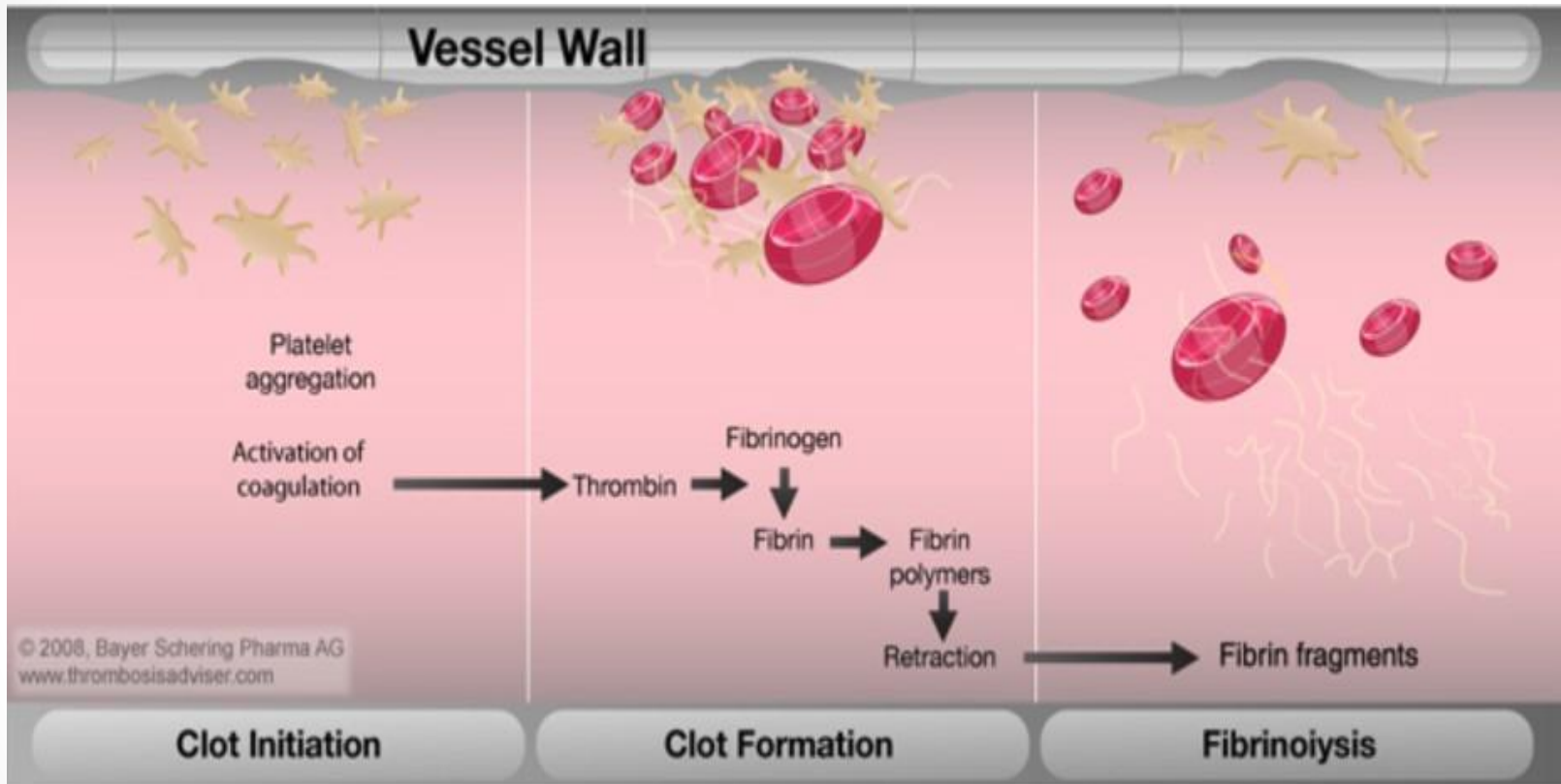
Uses :

Tissue Plasminogen Activator (t-PA) used to activate plasminogen to dissolve coronary clots.



• Plasmin inhibitors and activators keep it under control.

Hemostasis mechanisms



[Overview of hemostasis](http://www.youtube.com/watch?v=HqTRoesu8M)

[http://www.youtube.com/watch?v= HqTRoesu8M](http://www.youtube.com/watch?v=HqTRoesu8M)

❖ Bleeding disorders:

- Platelets defects
- Coagulation factors defect

e.g. hemophilia:

X-linked disease which affects male, 85% is due to **FVII** deficiency (hemophilia A), 15% is due to **FIX** deficiency (hemophilia B)

- Vit.K deficiency & liver disease:

Almost all coagulation factors are synthesized in the liver.

Prothrombin, FX, FIX & FVII require vitamin K for their synthesis

Check your understanding!

<http://www.onlineexambuilder.com/physiology-homeostasis/exam-11388>

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