HLS

MODIFIED NO. 5

PHYSIOLOGY

كتابة: ميس سلمان ، زين مالك

تدقيق: ميس العتيق

الدكتور: إباء زيادنة

UNIT VI

Hemostasis and Blood Coagulation

Ebaa M Alzayadneh, PhD

Associate Professor of Physiology

Color code

- Slides
- Doctor
- Additional info
- Important

The function of blood elements that are concerned with stopping bleeding is mainly carried out by the platelet's function and also with certain factors.

Events in Hemostasis

Vascular Constriction

- Local myogenic spasm-most effective
- Local autacoid factors
- Nervous reflexes-from pain receptors

Formation of a Platelet Plug

- Small cut in a vessel; have a plug
- instead of the complete clotting mechanism

The hemostasis mechanism of our body (hemo: blood and stasis: stop(

1st step: vascular constriction:

Due to ↓ bleeding by ↓ diameter ↓ blood flow and that will happen in three ways:

1(local myogenic spasm-automatically: the smooth muscle in the vessel wall contracts.

2(Local autacoid factors :the local factors will be released by injured tissue.

3(Nervous reflexes: induced by pain/sensory nerve fibers.

2nd step: Formation of platelet plug:

There is no attachment between the surface of platelets and the surface of endothelial tissue of vessels in a normal situation but, where there is a cut in a blood vessel, the attachment will be happened between the surface of platelets and exposed collagen fibers or exposed connective tissue that lines the endothelial tissue.

This contact activates platlets by
-changing the structure (becoming irregular, swelling, and pseudopodia shape(

-releasing granules to activate other platlets.

Formation of plug is done ✅

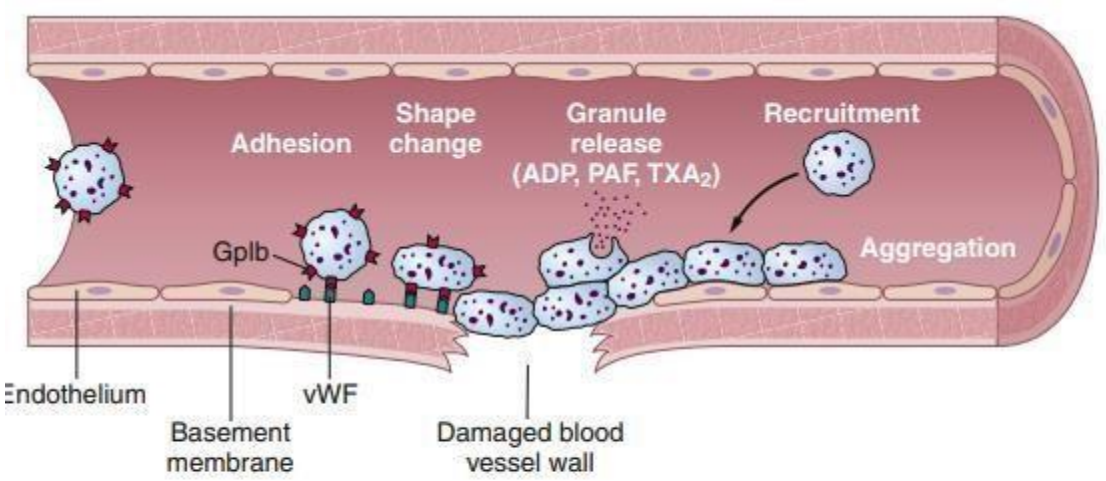
The plug is sufficient if the cut is very small, but it will be strengthened with other factors/building blocks as fibrin to make stronger meshwork.

Formation of clot

3rd step: Blood clotting

In coming slides

Platelet Plug Formation



Von Willebrand factor (vWF) serves as an adhesion bridge between subendothelial collagen-exposed collagen - and the glycoprotein Ib (GpIb) platelet receptor.

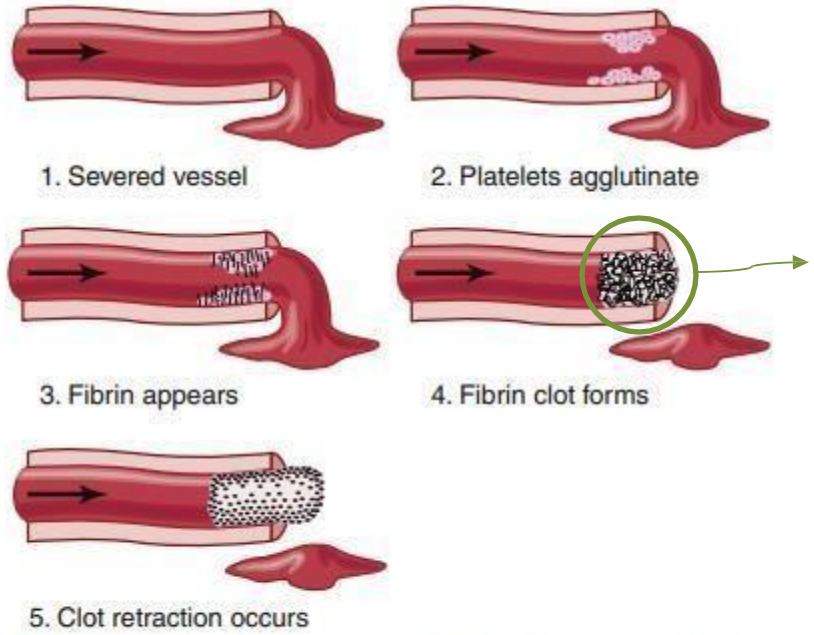


Figure 37-2. Clotting process in a traumatized blood vessel. *(Modified from Seegers WH: Hemostatic Agents. Springfield, IL: Charles C Thomas, 1948.)*

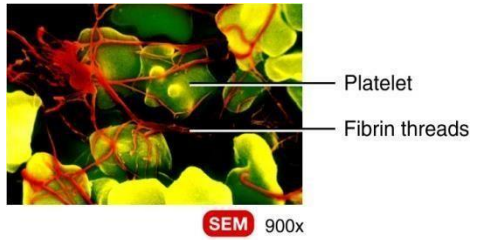
Von Willebrand factor is found within the plasma and is essential for specific localization to the cut edges.

Extra:

Blood Clotting

3. Blood clotting
   - Serum is blood plasma minus clotting proteins
   - Clotting – series of chemical reactions culminating in formation of fibrin threads
   - Clotting (coagulation) factors – Ca^{2+}, several inactive enzymes, various molecules associated with platelets or released by damaged tissues

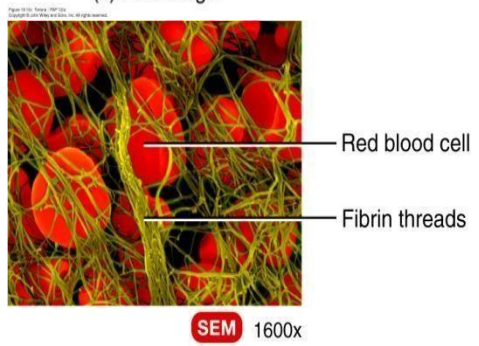
Platelets are equipped with various enzymes, coagulation factors, and energy molecules essential for coagulation. Although they are not cells, they contain remnant of the rough endoplasmic reticulum (RER), Golgi apparatus, and mitochondria, which contribute to their function. However, their half life is very short (8-12) days .



(a) Early stage

(b) Intermediate stage

(c) Late stage



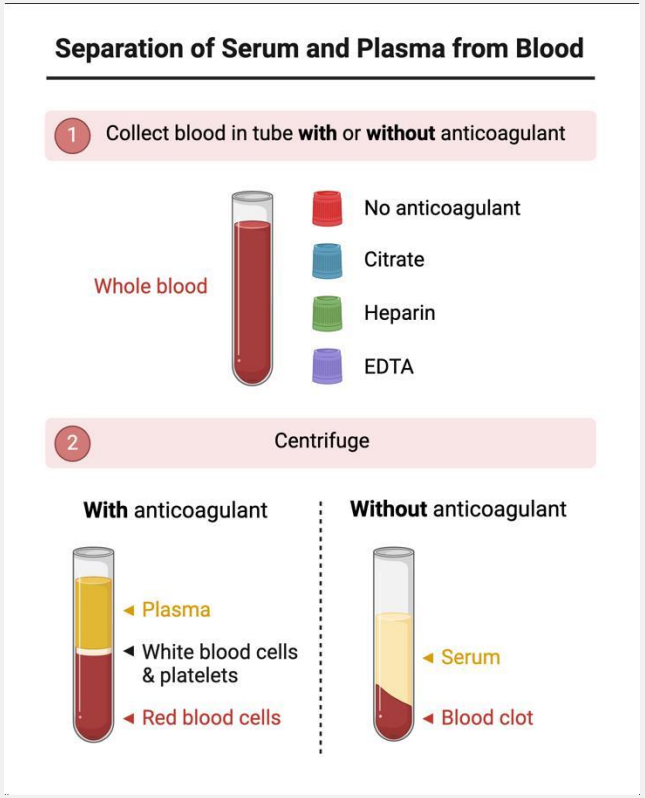
(d) Red blood cells trapped in fibrin threads

When you put the blood in a tube without anticoagulant, the blood will change its structure because the platelets will be activated in an injury state due to they are outside vessels.?neppah seod tahw….

A: the fibrinogen and other coagulant factors will be activated in the button of the tube with RBCs and the plasma becomes without these factors so we call it “serum.”

There are 12 coagulant factors should be activated in plasma and platelets and this activation only happens when the platelets are activated.

Extra image:

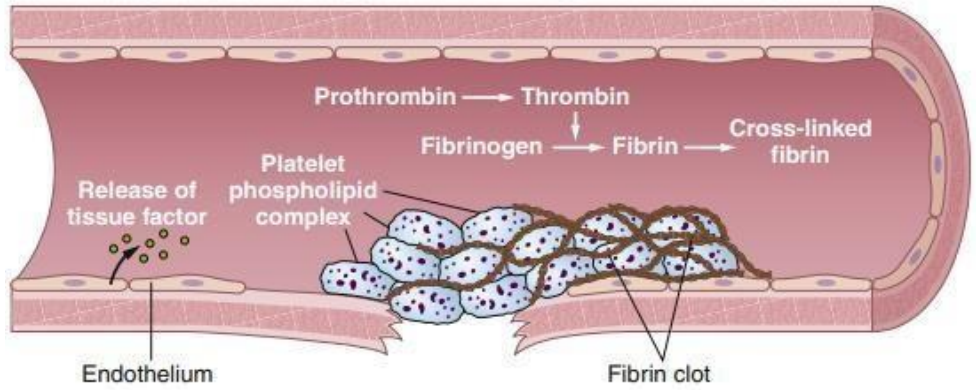


Blood Clotting

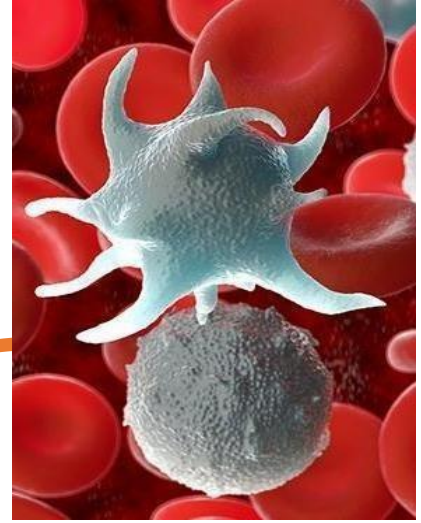
Tissue factor is released when tissue is involved in an injury. If the tissue is not involved, no tissue factor will be released.

- Exposure of blood to vasc wall- release of TF (tissue factor) also named (III or thromboplastin) from endo cells , phospholipids(either from the damaged tissue membrane or platelets membrane) that activate multiple stages in the blood-clotting process., thrombin activation- ----------Fibrin

Exposure of blood to the vascular wall leads to the release of tissue factor (TF), also known as thromboplastin (Factor III), from endothelial cells. Phospholipids, either from the damaged tissue membrane or platelet membranes, activate multiple stages in the blood-clotting process. This cascade ultimately results in the activation of thrombin, which converts fibrinogen to fibrin.



Events in Hemostasis



Platelets are fragmented as they exit capillaries into the bloodstream. However, some megakaryocytes also fragment within the bloodstream.

- **Platelets**
  - Fragmented megakaryocytes; after released via capillaries
  - 150,000-300,000
  - Do not have nuclei and cannot reproduce
  - Contain actin and myosin (thrombosthenin) (contractile proteins)
  - Mitochondria-Produce ATP that provide energy for the activation of enzymes involved in the coagulation steps.
  - Release prostaglandins
  - Release endothelial cell growth factor for the repair process after an injury
  - Surface glycoproteins for adherence to damaged Vessels
  - Half-live of 8-12 days

ADP also plays an important role in platelet adhesion and activation.

Events in Hemostasis

- **Mechanism of the Platelet Plug**

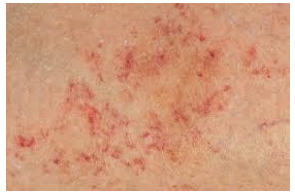
Once platelets approach the site of injury, they are attracted to exposed collagen or damaged endothelial cells and change their own characteristics

a. Platelets swell; irregular shape with pseudopods
b. Become sticky and adhere to collagen
c. Thromboxane A_2 and ADP enhance adherence
d. Damaged wall activates increasing numbers of platelets
e. Important in closing small tears or ruptures in very small vessels (petechiae)

Platelets adhere to collagen via von Willebrand factor (vWF). Upon activation, they release thromboxane A2 (TXA2) and ADP, which make them sticky and promote adhesion to other platelets.

We regularly injure our blood vessels, such as when we hit our hand against a wall. In response, platelets and other clotting factors are responsible for sealing these ruptures.

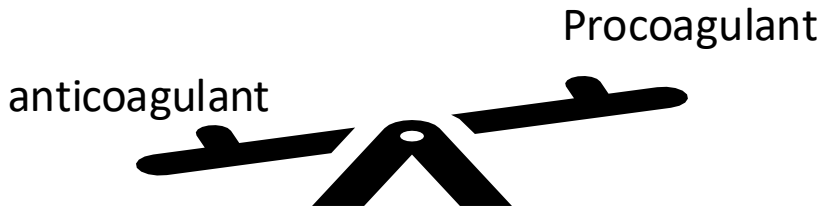
If there is an abnormality in platelet number or function, even small ruptures can appear as petechiae.



Blood Coagulation

- **Basic Theory**

a. Depends on the state of balance of 50 or more possible blood procoagulants and anticoagulants At physiological conditions, anticoagulants override procoagulants
b. Procoaglants overrides in the event of an injury but should be confined to the site of the injury., formation of prothrombin activator occurs, which subsequently activates thrombin.
c. Conversion of prothrombin to thrombin
d. Conversion of fibrinogen to fibrin



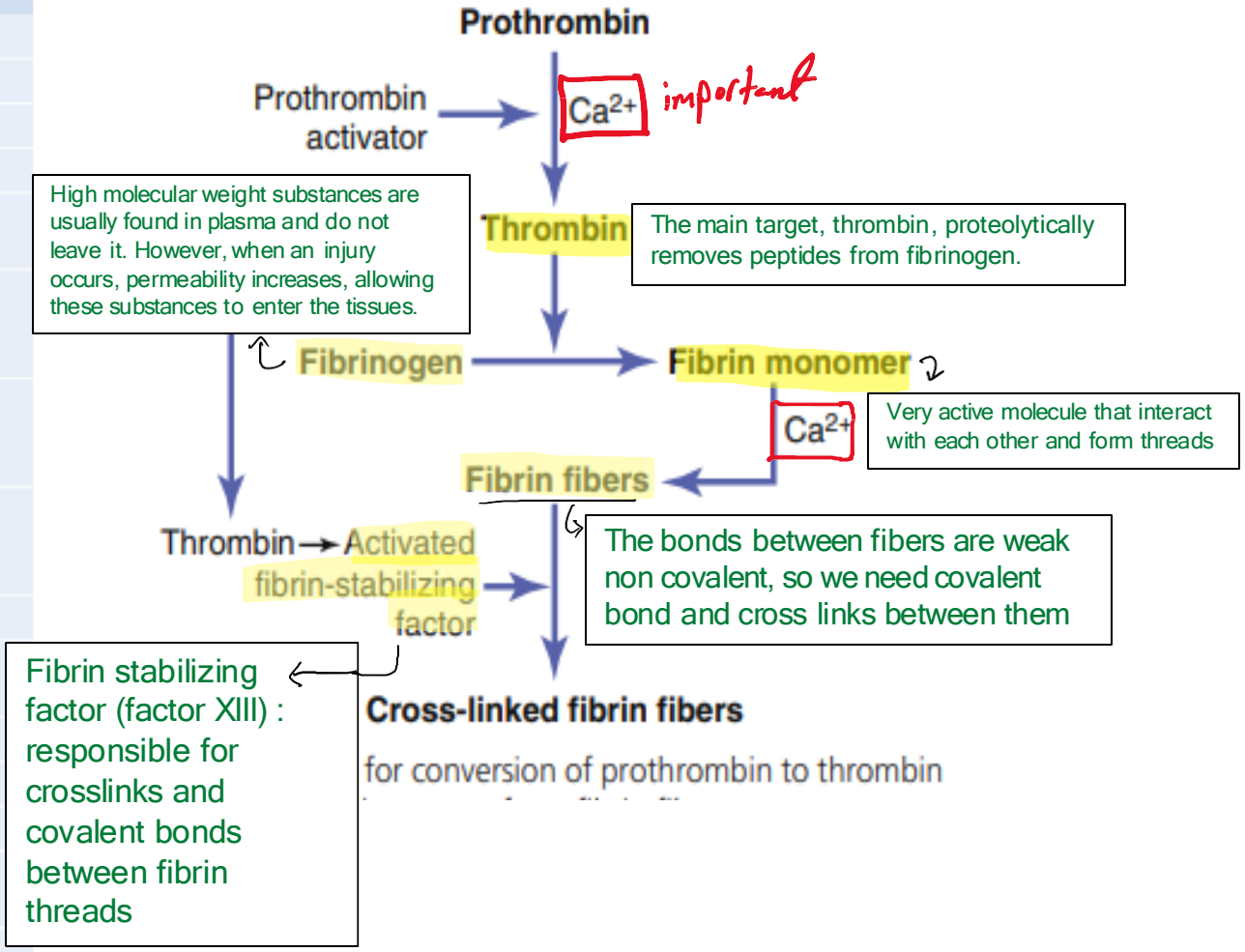
Clotting Factors

Table 37-1 Clotting Factors in Blood and Their Synonyms[a]

Clotting Factor	Synonym(s)
Fibrinogen	Factor I
Prothrombin	Factor II
Tissue factor	Factor III; tissue thromboplastin
Calcium	Factor IV
Factor V	Proaccelerin; labile factor; Ac-globulin (Ac-G)
Factor VII	Serum prothrombin conversion accelerator (SPCA); proconvertin; stable factor
Factor VIII	Antihemophilic factor (AHF); antihemophilic globulin (AHG); antihemophilic factor A
Factor IX	Plasma thromboplastin component (PTC); Christmas factor; antihemophilic factor B
Factor X	Stuart factor; Stuart-Prower factor
Factor XI	Plasma thromboplastin antecedent (PTA); antihemophilic factor C
Factor XII	Hageman factor
Factor XIII	Fibrin-stabilizing factor
Prekallikrein	Fletcher factor
High-molecular-weight kininogen	Fitzgerald factor; high-molecular-weight kininogen (HMWK)
Platelets	

[a]These are listed here mainly for historical interest.

Very famous
Absence of it cause hemophilia



3 Stages of Clotting

Obtaining thrombin is not straightforward, as different pathways collaborate based on the severity of the injury. There are two pathways to produce thrombin: the extrinsic pathway and the intrinsic pathway.

1. Extrinsic or intrinsic pathway lead to formation of prothrombinase
2. Prothrombinase converts prothrombin into thrombin
3. Thrombin converts fibrinogen (soluble) into fibrin (insoluble) forming the threads of the

Thus, the rate-limiting factor in causing blood coagulation is usually the formation of prothrombin activator

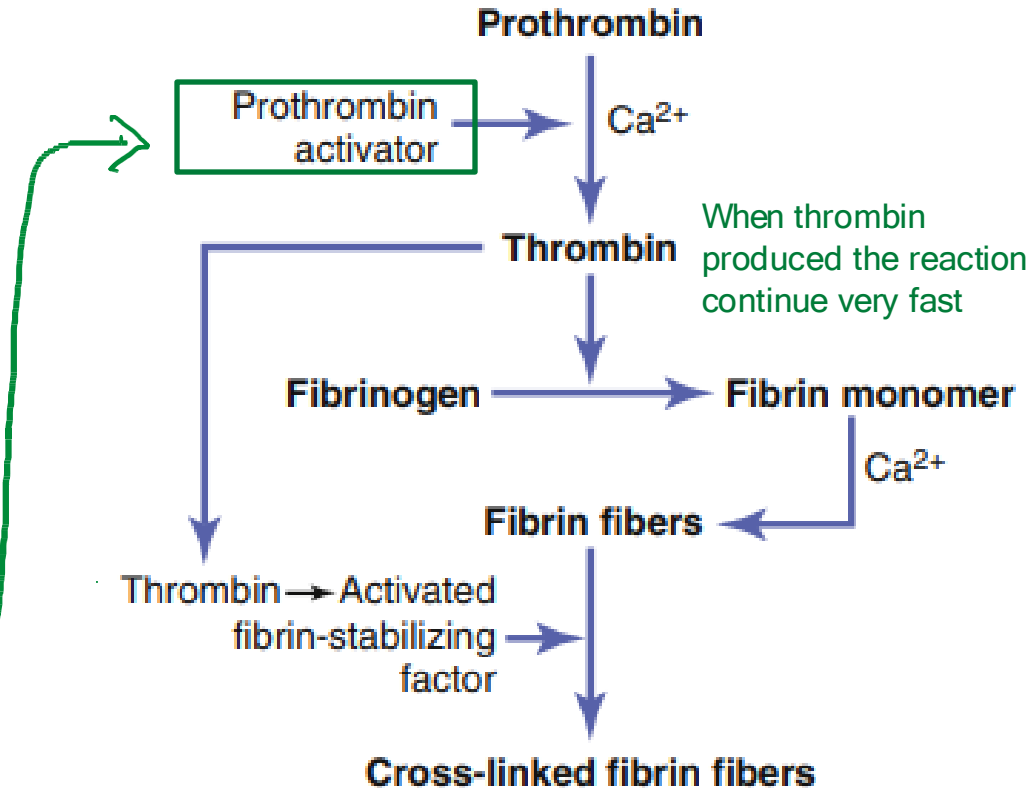


Figure 37-3 Schema for conversion of prothrombin to thrombin

Hemostasis: Prevention of Blood Loss

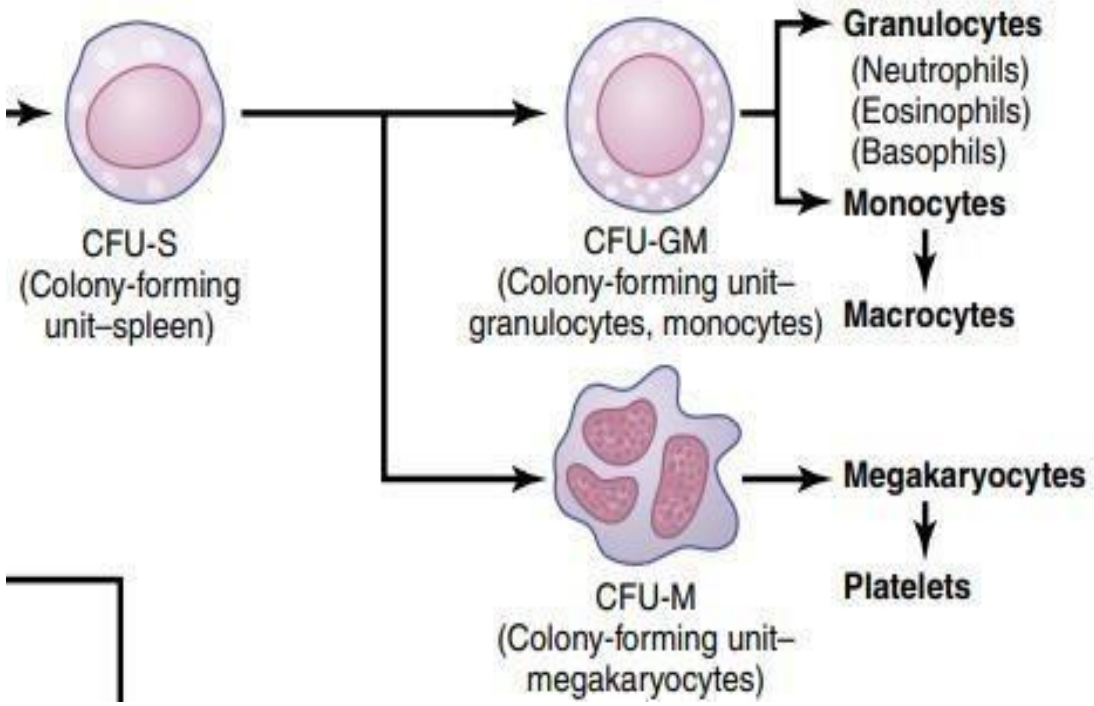
- **Vascular constriction**
- **Formation of a platelet plug**
- **Formation of a blood clot**
- **Healing of vascular damage ± re- canalization**

Vascular Constriction

- **Myogenic spasm**
- **Local autocoid factors from damaged tissues and platelets**
- **Nervous reflexes**
- **Smaller vessels: thromboxane A_2 released by platelets**

Platelets (Thrombocytes(

- 1- 4 µm discs
- Released by fragmentation of megakaryocytes
- 150-300,000 per µL
- Half-life in blood of 8-12 days



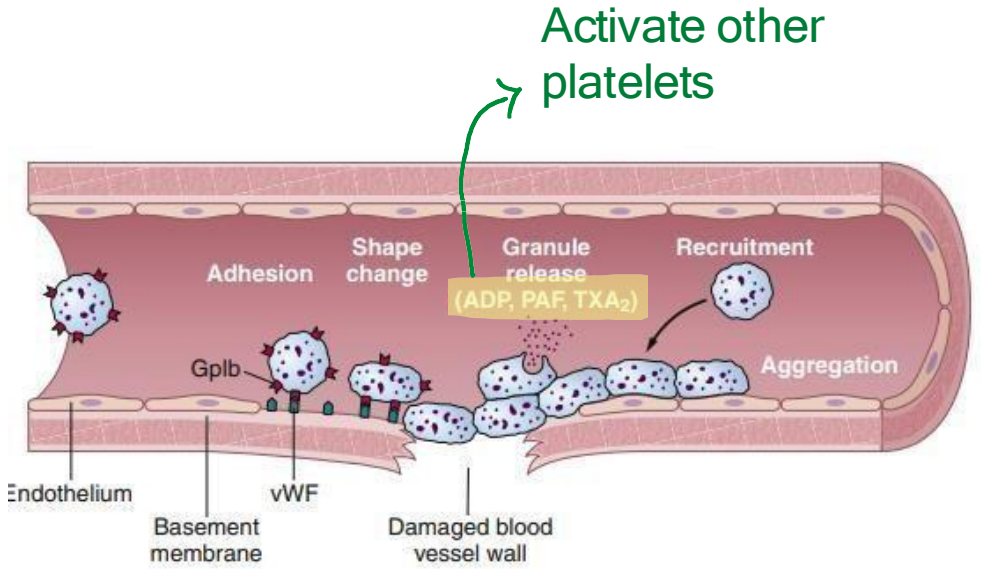
Platelet Functions

- Contractile capabilities
  - actin, myosin, thrombosthenin

- Residual ER and Golgi
  - synthesize enzymes, prostaglandins,

  fibrin-stabilizing factor, PDGF (Platelet-Derived Growth Factor), store Ca++ in mitochondria, glogi, and ER

- Mitochondria / enzymes
  - produce ATP, ADP



TO SUM UP ☺

Hemostasis means : prevention of blood loss

It can be achieved by several mechanisms

Vascular constriction

Result from :
- Local myogenic spam
- Local autacoid factors , vascular endothelium and platelets by release of TXA2
- Nervous reflexes

Formation of platelet plug

Steps:
- Adhesion: Platelets swell, form pseudopods, and bind to von Willebrand factor (vWF) through their glycoprotein receptors (GpIb).
- Activation: Activated platelets secrete increased quantities of ADP and platelet-activating factor (PAF), which further activate other platelets, along with thromboxane A2 (TXA2), a vasoconstrictor.
- Aggregation: This activation increases the number of platelets and attracts more platelets to form a platelet plug.

low platelets → petechaiae

Formation of platelet clot

A series of coagulation factors are activated through the intrinsic and extrinsic pathways, leading to the formation of prothrombin activator. This activator then converts prothrombin to thrombin, which converts fibrinogen to fibrin, stabilizing the clot and preventing further bleeding.

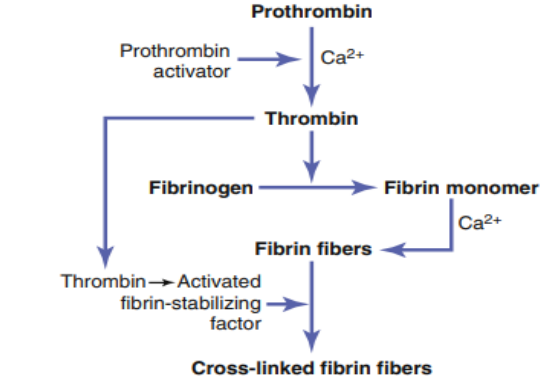
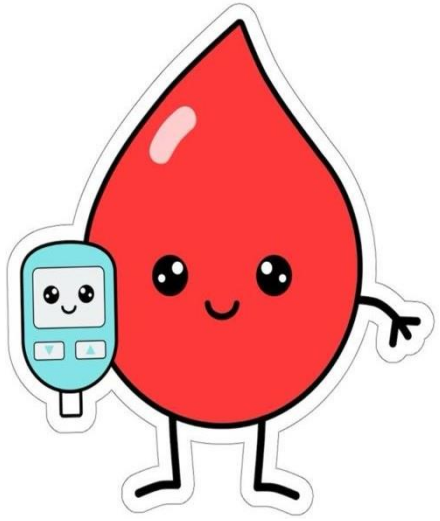


Figure 37-3 Schema for conversion of prothrombin to thrombin

Growth of fibrous tissue



Additional sources

1. GUYTON AND HALL CH 37
2. https://youtube.com/playlist?list=PL90EE5
   4545509447E&si=tigUCBQjbGv7vC2v

VERSIONS	SLIDE #	BEFORE CORRECTION	AFTER CORRECTION
V1→ V2	6	Life span is 8-12	Half life is 8-12
V2→V3			