Anatomy and Physiology

For

The First Class

2nd Semester

HEMATOLOGIC SYSTEM

Thrombocytes = Platelets

Thrombocytes = Platelets

- Blood platelets are non-nucleated disc like cell fragments 2-4 µm in diameter.
- Platelets are not true cells. They originate from fragments of megakaryocyte cytoplasm that reside in the red bone marrow.
- Each platelet has a peripheral light blue stain transparent zone the **hyalomere** and a central zone containing granules called the **granulomere**.

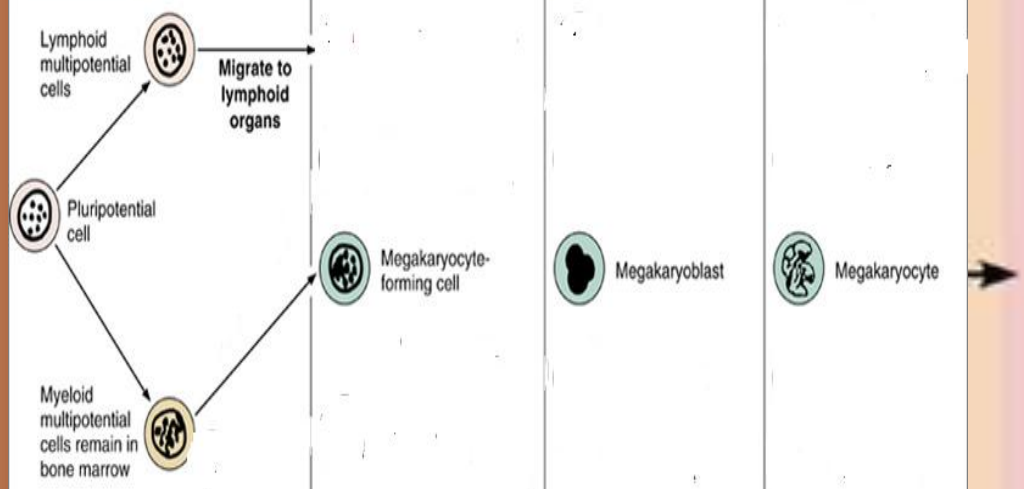
- Platelets granules contain *calcium ions*, *ADP*, *ATP*, *serotonin*, *pyrophosphate*, *hydrolytic enzymes*, *P- selectin*, *fibrinogen*, *platelet-derived growth factor, coagulation factor V and XIII and other substances.*

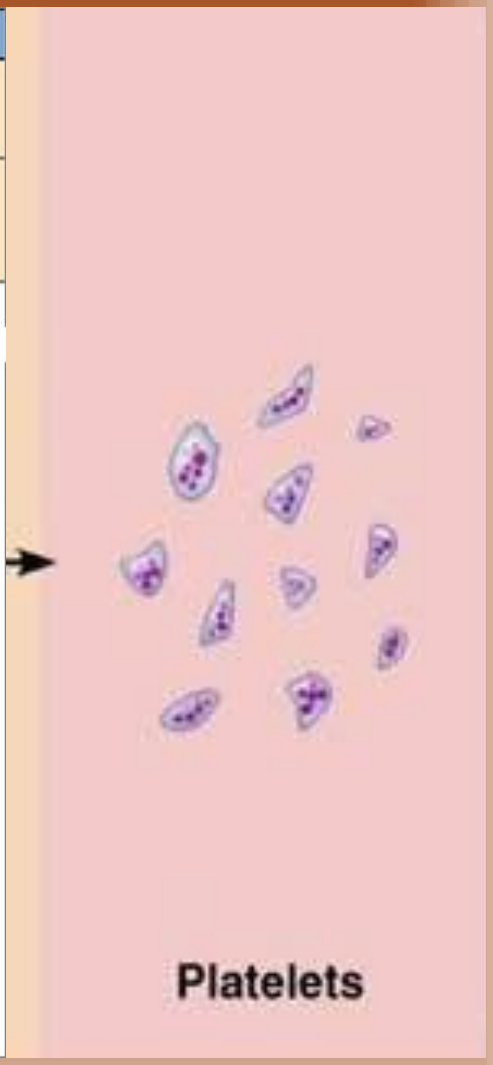
- *Platelets are very sticky so appear under light microscope as clumps of cells.*

- Platelets promote blood clotting and help repair gaps in the walls of blood vessels, preventing loss of blood.
- Normal platelets counts range from 200,000-400000 per microliter of blood.
- **Thrombopoietin** released by kidneys has ability to stimulate platelets synthesis.
- Platelets have a life span of about **10 days**.

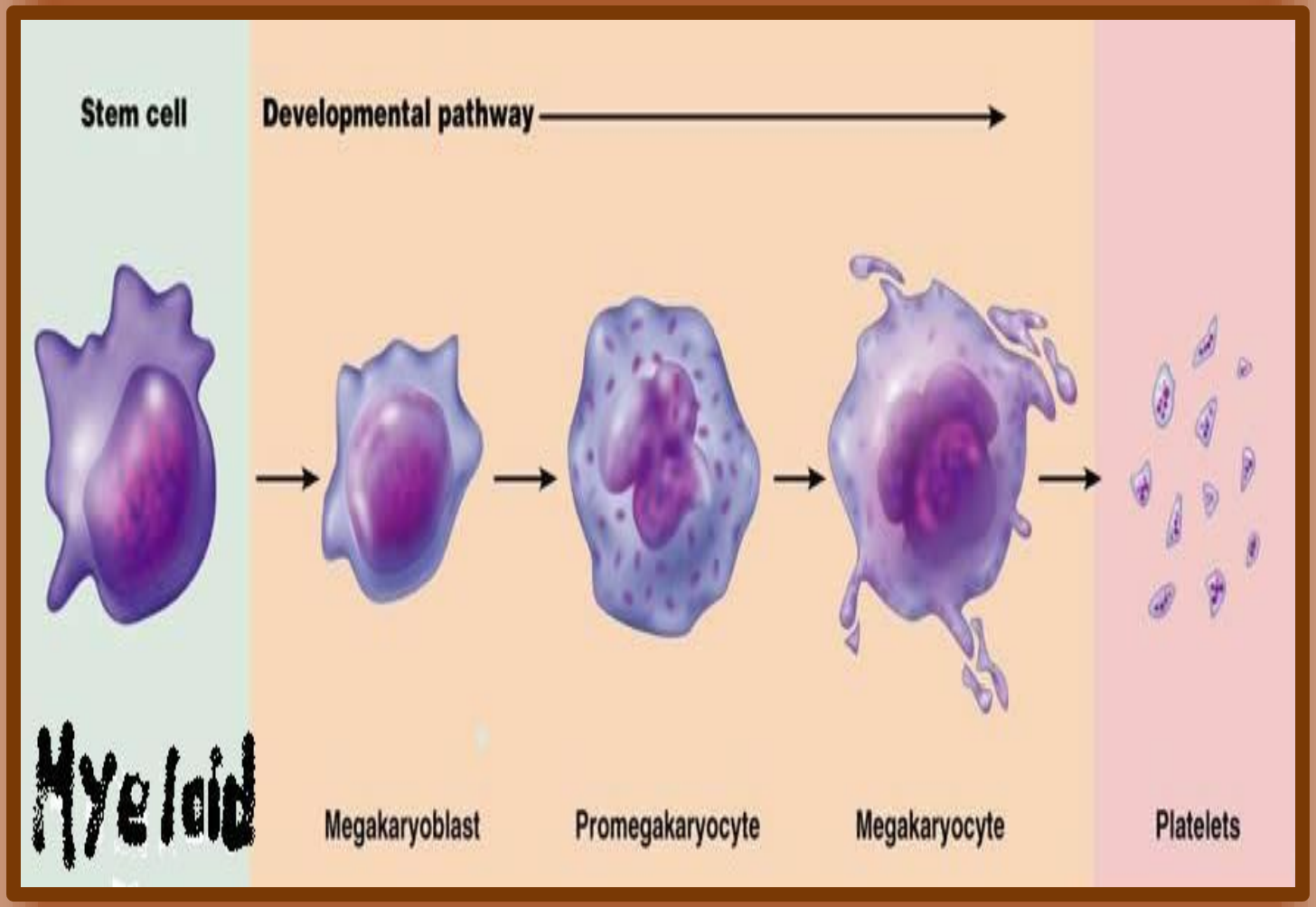
Thrombopoiesis

Phase	Stem Cells	Progenitor Cells	Precursor Cells (Blasts)	Mature Cells
Early morphologic	Not morphologically distinguishable; have the general aspect of lymphocytes		Beginning of morphologic differentiation	Clear morphologic differentiation
Mitotic activity	Low mitotic activity; self-renewing; scarce in bone marrow	High mitotic activity; self-renewing; common in marrow and lymphoid organs; mono- or bipotential	High mitotic activity; not self-renewing; common in marrow and lymphoid organs; monopotential	No mitotic activity; abundant in blood and hematopoietic organs

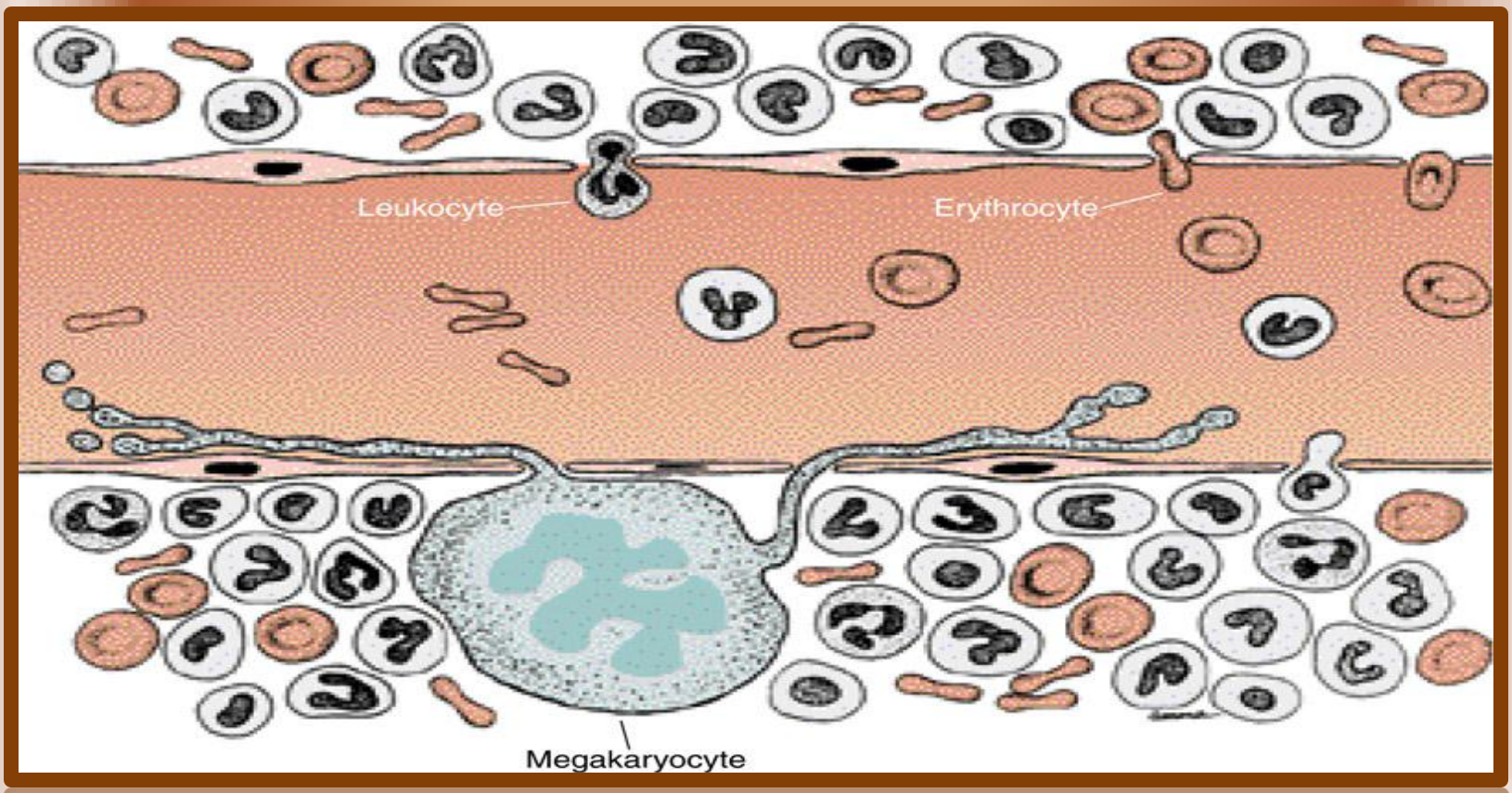




Thrombopoiesis



Drawing showing the passage of erythrocytes, leukocytes, and platelets across a sinusoid capillary in red bone marrow. Because erythrocytes (unlike leukocytes) do not have sufficient motility to cross the wall of the sinusoid, they are believed to enter the sinusoid by a pressure gradient that exists across its wall. Leukocytes, after the action of releasing substances, cross the wall of the sinusoid by their own activity. Megakaryocytes form thin processes that cross the wall of the sinusoid and fragment at their tips, liberating the platelets.

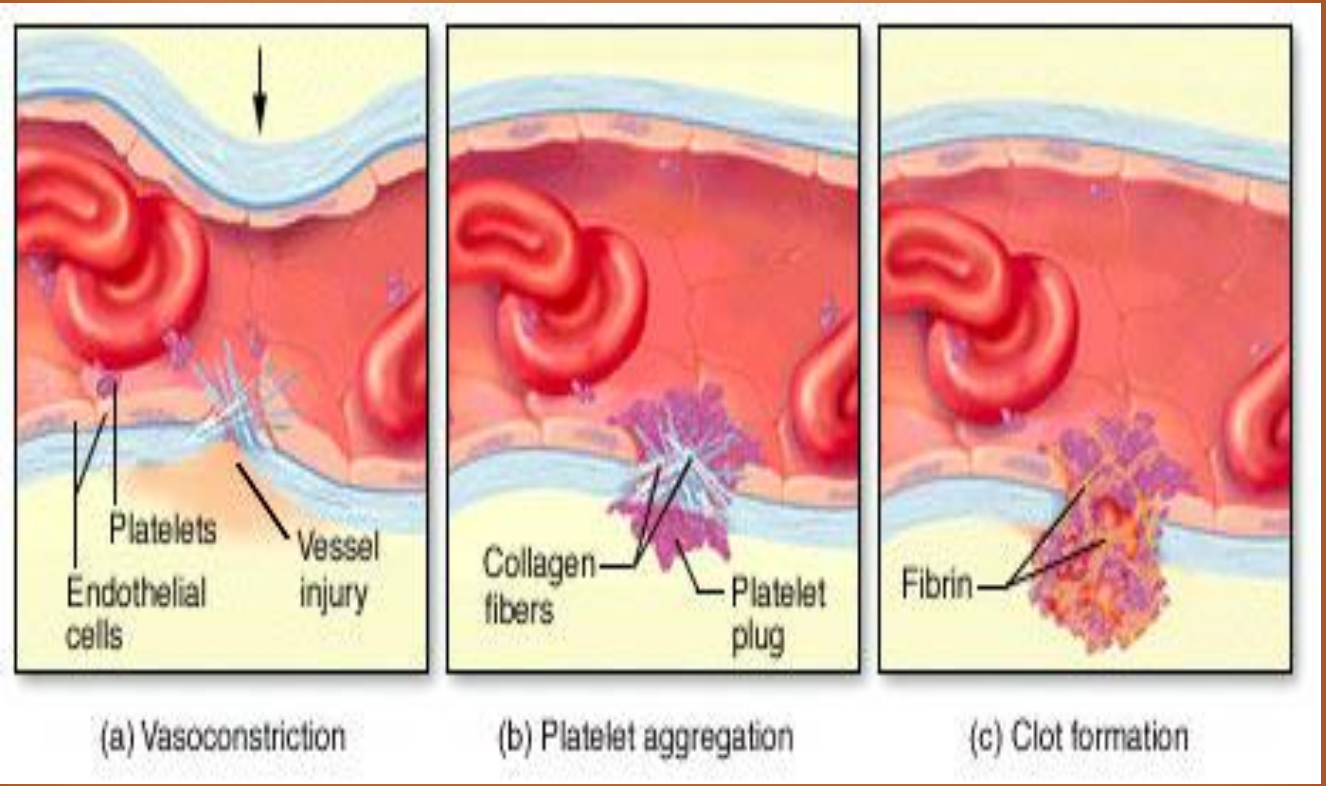


Haemostasis= Hemostasis

Steps of Haemostasis

1. Vascular spasm
2. Platelets plug formation
3. Coagulation (blood clotting)
4. Fibrynolysis

Steps of Hemostasis



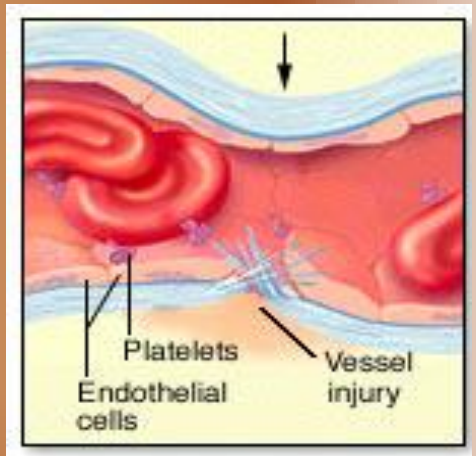
1. Vascular spasm

Cause by:

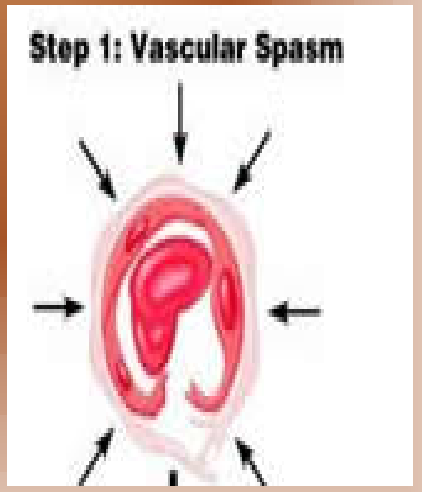
- **Direct injury** (vasoconstriction specially in the area where damage took place).

- **Chemical substances** (like **serotonin** produced by platelets that aggregate on damaged blood vessel and **thromboxanes** released by damaged vessel).

- **Pain reflex**



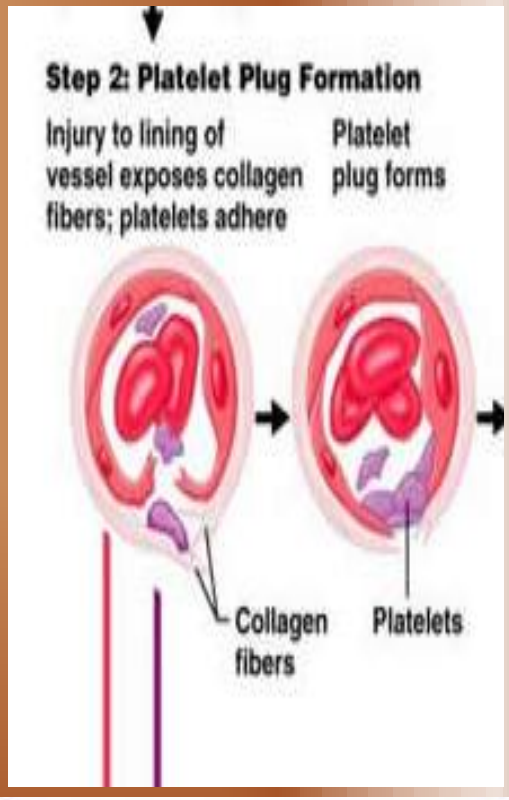
(a) Vasoconstriction

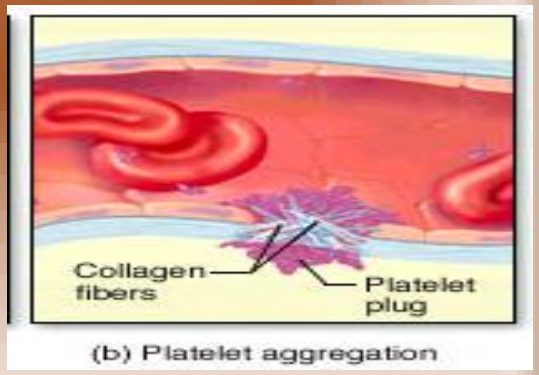


Platelets plug formation

1. **Primary aggregation**: discontinuities in the endothelium are followed by platelets aggregation to exposed collagen. Thus, a platelet plug is formed at a first step to stop bleeding.

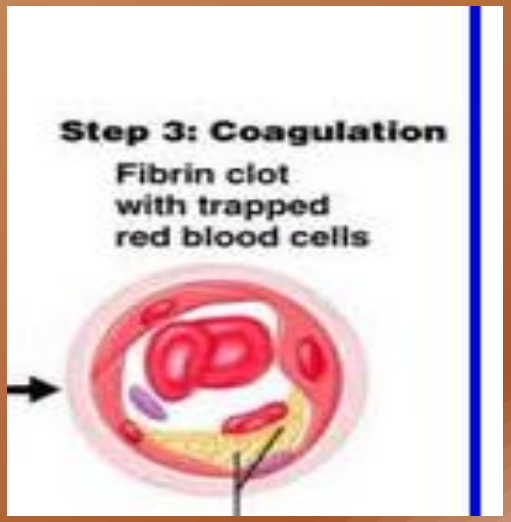
2. **Secondary aggregation**: platelets in the plug release an adhesive glycoprotein and ADP. Both are potent platelet aggregation, increasing the size of the platelets plug.

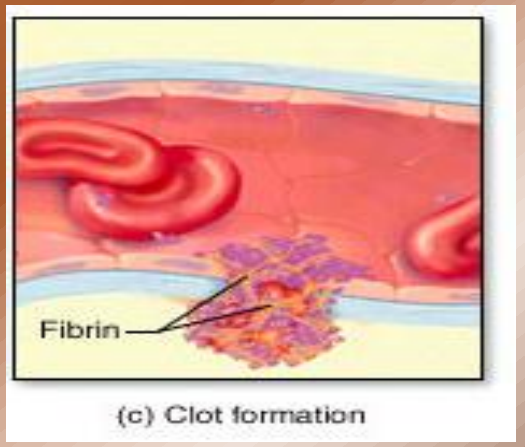




3. Coagulation (blood clotting)

- Coagulation of blood is very important for stoppage of bleeding from an injured blood vessel. The process of coagulation is complex and involves many steps and many factors (most of which is proteins). The factors are identified by roman numerals (I – XIII), and also given names as shown in the next slide.
- These clotting factors activate each other in specific order resulting in the formation of ***prothrombin activator.***
- ***Prothrombin activator*** is the first step in the *final common pathway* of blood coagulation.
- In the final common pathway, the prothrombin activator converts **prothrombin** (present in the plasma) to **thrombin** (an enzyme).
- Thrombin acts on the plasma protein **fibrinogen** and converts it into insoluble fibers of **fibrin** these fibers form a meshwork in which blood get entangled to form a sold clot.



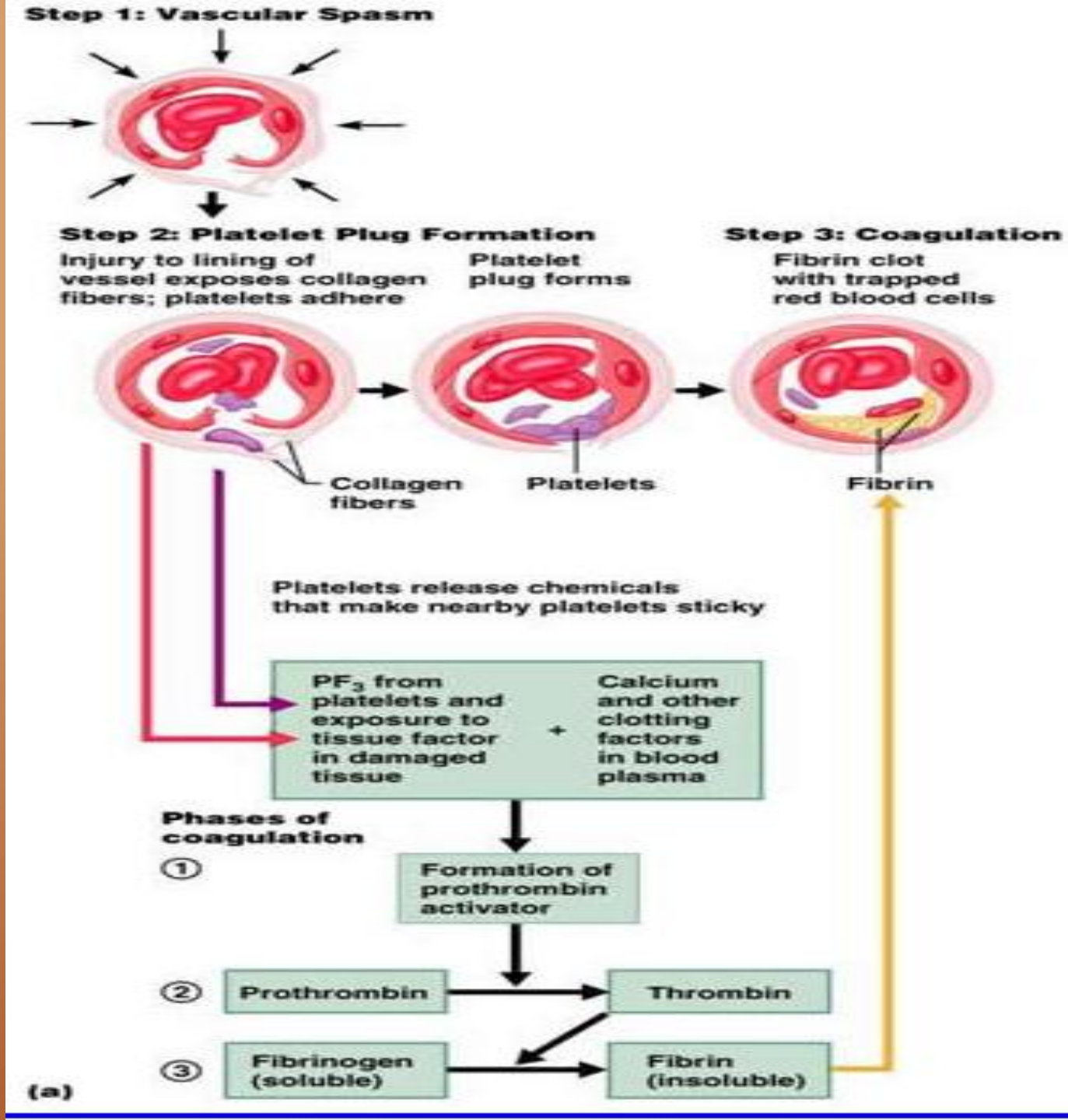


Blood Clotting Factors

- **I** = Fibrinogen
- **II** = Prothrombin
- **III** = Tissue factor (thromboplasin)
- **IV** = Calcium Ions
- **V** = Labile factor, proaccelerin, Ac- globin
- **VI** = It now believed to be same as factor V
- **VII** = stable factor, proconvertin
- **VIII** = Antihemophilic facter A
- **IX** = Antihemophilic factor B
- **X** = Stuart Prower factor (thrombokinase)
- **XI** = Antihemophilic factor C
- **XII** = Hagman factor
- **XIII** = fiber stabilizing factor

Vitamin K is essential for synthesis of factors **II, VII, IX, and X.**

Steps of Haemostasis



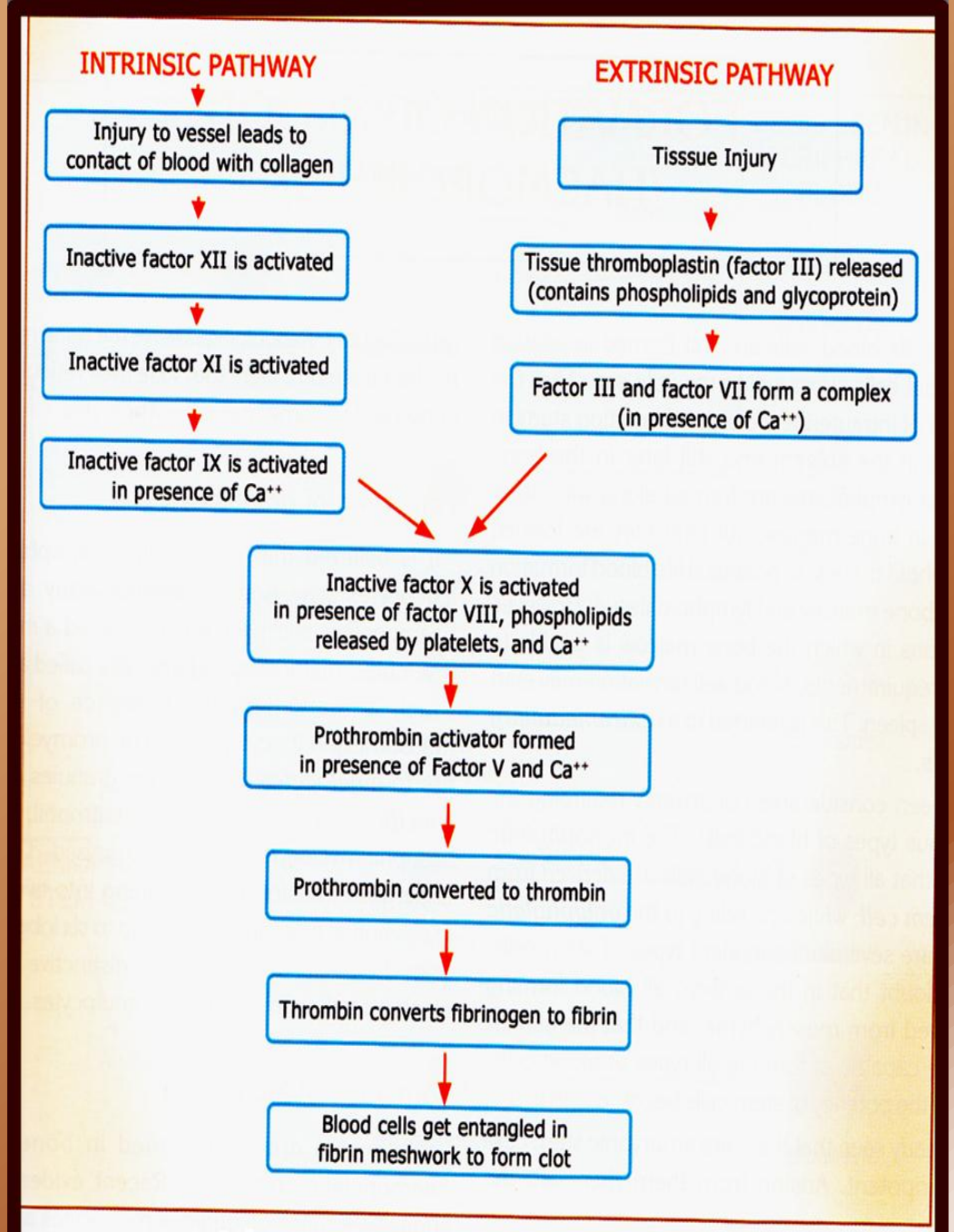
The fibrin meshwork

- The final common pathway can be initiated by two processes (pathways):

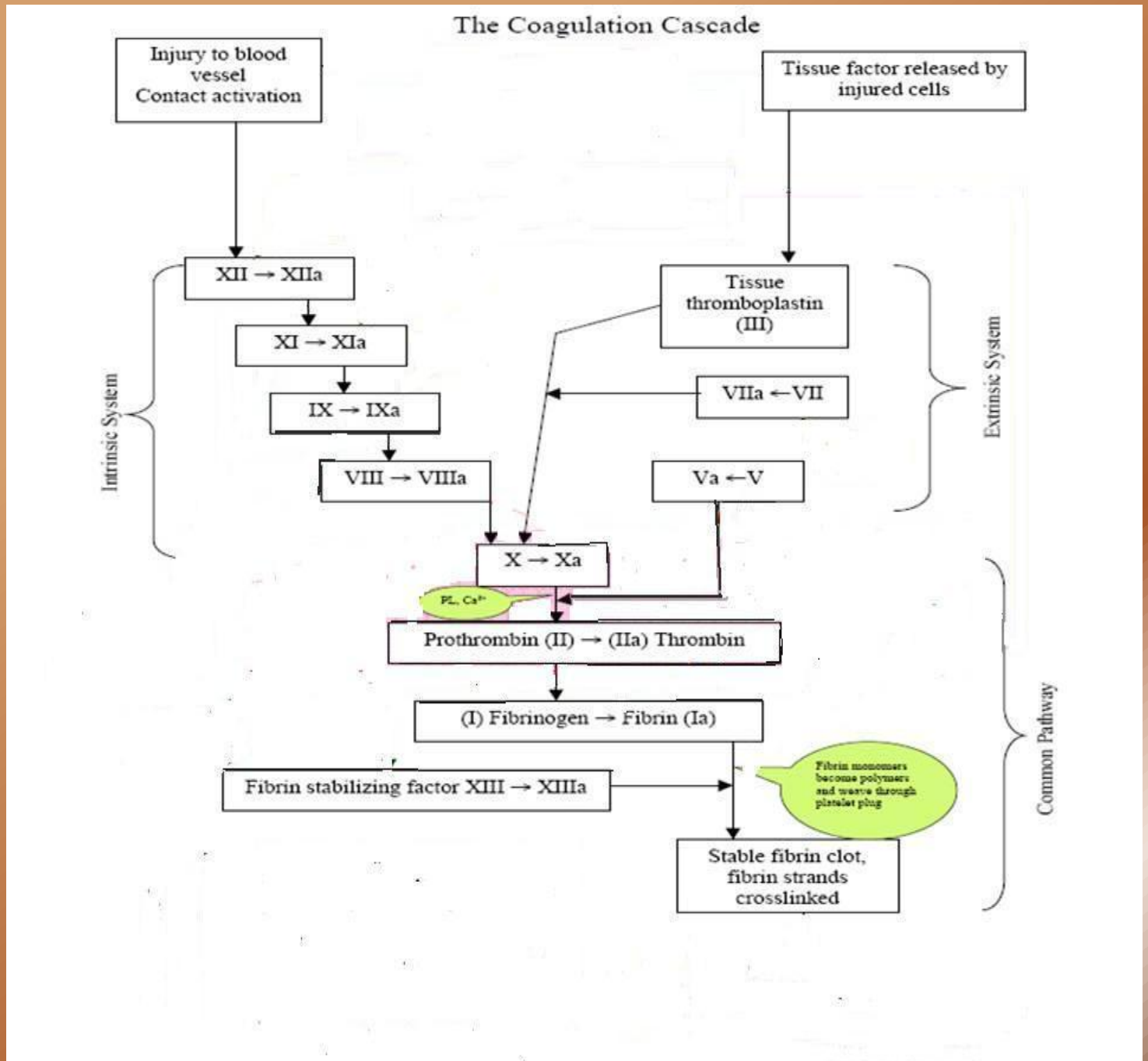
1. Extrinsic pathway occurs due to tissue damage.

2. Intrinsic pathway occurs due to damage to endothelial cells.

Each pathway consists of a number of steps that are shown in the next slides.

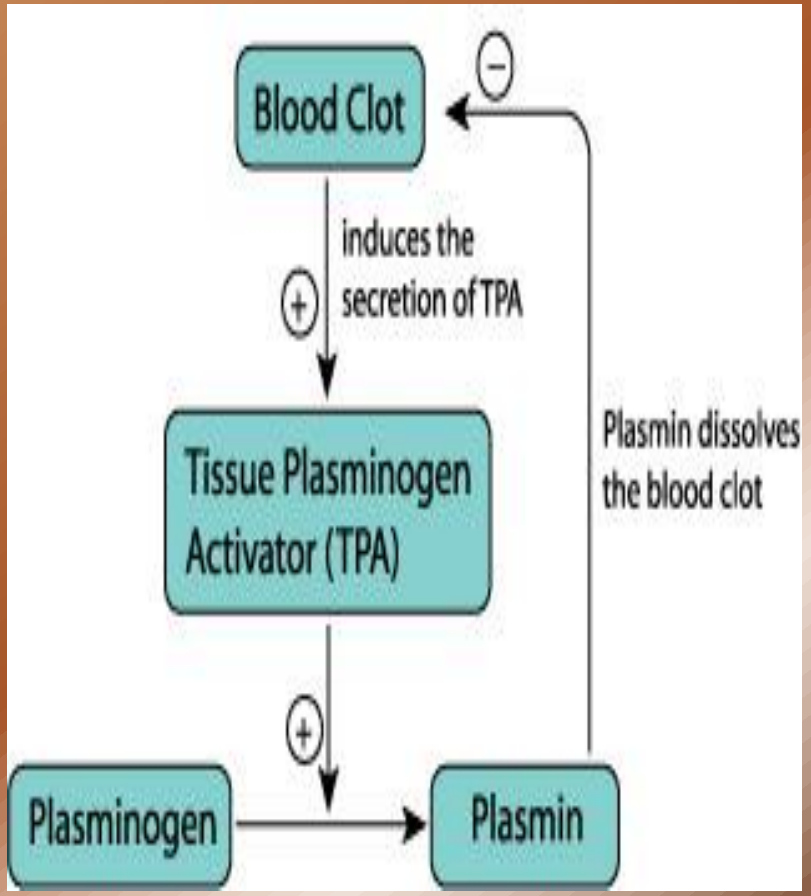


Pathways for generation of prothrombin factor.


The Coagulation Cascade
Injury to blood vessel Contact activation
Tissue factor released by injured cells
XII → XIIa
XI → XIa
IX → IXa
VIII → VIIIa
Tissue thromboplastin (III)
VIIa ←VII
Va ←V
Intrinsic System
Extrinsic System
X → Xa
PL, Ca++
Prothrombin (II) → (IIa) Thrombin
(I) Fibrinogen → Fibrin (Ia)
Fibrin stabilizing factor XIII → XIIIa
Fibrin monomers become polymers and weave through platelet plug
Stable fibrin clot, fibrin strands crosslinked
Common Pathway

Fibrinolysis

- After the clot has formed the process of removing it and healing the damaged blood vessel begins.
- Fibrinolysis (breakdown of the clot) is the first step of healing.
- Plasminogen is converted to the plasmin.
- Plasmin intiates the breakdown of fibrin to soluble.
- As the clot is removed the healing process restores the integrity of the blood vessel wall.



Control of Coagulation

- The body control and limit the coagulation cascade; otherwise once started the clotting process would spread throughout the circulatory system. The main controls are:

1. The perfect smoothness of normal endothelial cells of the blood vessel (means that platelets do not adhere to it.
2. The presence of natural anticoagulants, e.g. heparin in the blood which inactivate clotting factors.