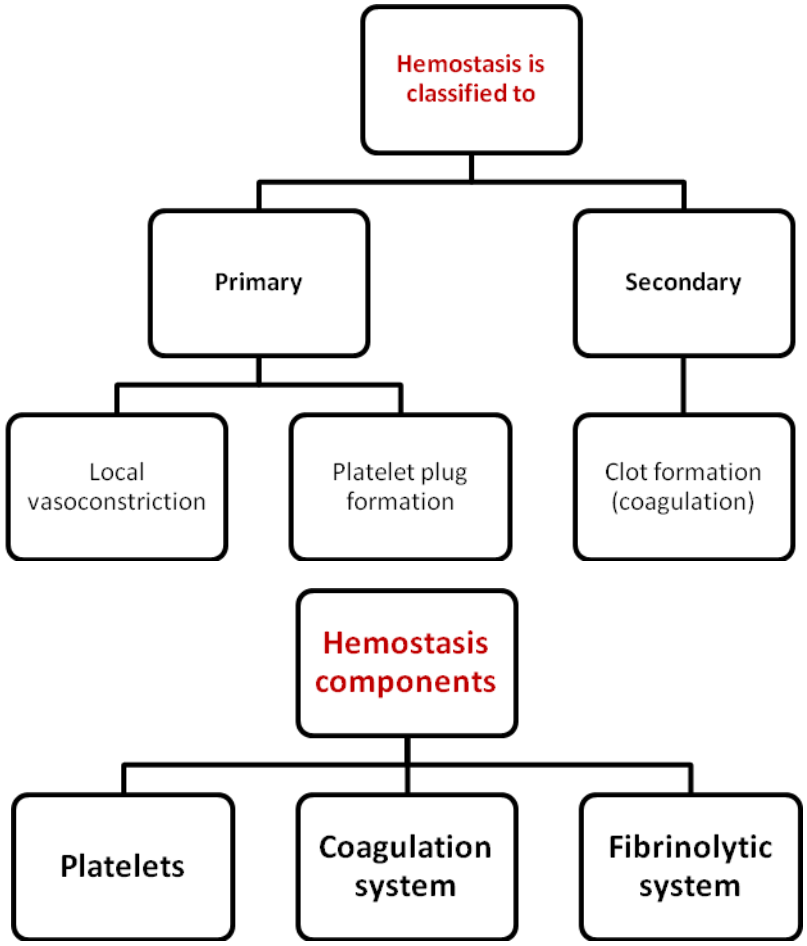
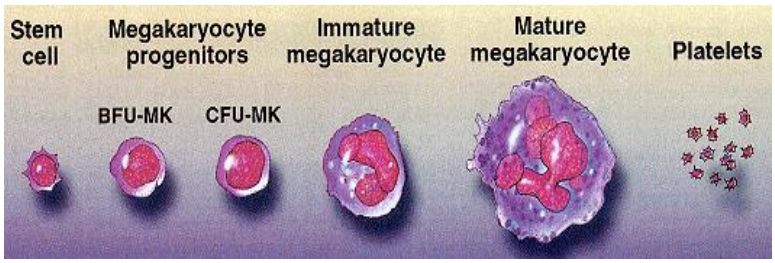


- **Platelet production:**

  PHSC → BFU-MK → CFU-MK → Immature Megakaryocytes → Mature megakaryocytes → by shedding their cytoplasm they will give rise to multiple platelets (each MK can give rise to 1000-5000 platelets).

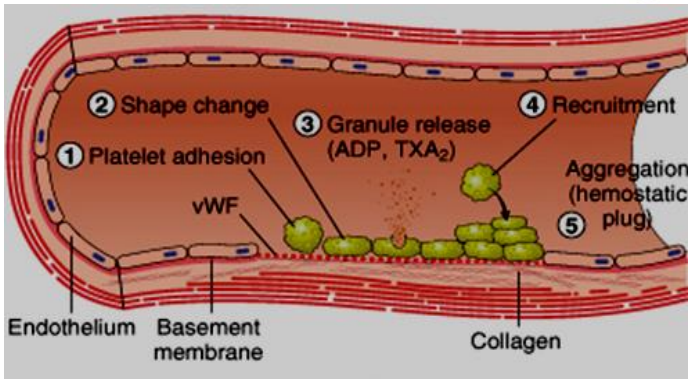
  Note: this production of platelets is regulated by thrombopoietin which is produced by the liver and kidneys.



- **Platelet characterizations:**
  - They are very flexible, discoid in shape, but changing their shape according to their function and the area of injury which they must cover.
  - Normally their lifespan is 7-10 days. Then, they will be removed from the circulation by macrophages of the RE system (mainly present in spleen & liver).
- **Platelet contents:**
  - The platelets contain three types of storage granules:
    - ✓ Dense granules: they contain ADP, calcium & serotonin.
    - ✓ α-granules: they contain clotting factors, VWF, PDGF and other proteins.
    - ✓ Lysosomes: they contain hydrolytic enzymes.
- **Vasoconstriction:**
  - First event to occur when there is injury to blood vessels (ex.cut) and it aims to reduce blood flow through the vessel and thus preventing further blood loss.
  - It is caused by:

- ✓ Nervous stimulation of α_2-receptors.
- ✓ And the release of different vasoactive substances such as 5-HT & thromboxane A_2.

- **Platelet plug formation:**
  - Damage to the intima of blood vessel → basement membrane is exposed (collagen & VWF) → platelets adhesion will occur via attachment of GPIa to collagen and GPIIb/IIIa & GPIb to VWF → platelets will change their configuration to cover more area of injury → platelets will aggregate by the attachment of their active GPIIb/IIIa recpetors to fibrin bridges (coming from the coagulation cascade)→ platelets will release ADP & TXA2 to activate more platelets



- **Coagulation cascade:**

Extrinsic pathway	Intrinsic pathway
Activated within seconds (15s)	Activated within minutes (2-6 min)
Triggered by: tissue trauma	**Triggered by**: blood trauma or contact with collagen
Cascade: Tissue injury → Release of tissue factor (TF) → TF binding to factor VIIa → Formation of factor Xa → Factor Xa acting with factor V to form prothrombin activatior → Conversion of prothrombin to thrombin → Thrombin will convert fibrinogen to fibrin.	**Cascade**: Blood trauma or contact with collagen → formation of factor XIIa → Formation of factor XIa → formation of factor IXa → factor IXa with factor VIII will activate factor X anf form factor Xa → Factor Xa acting with factor V to form prothrombin activatior → Conversion of prothrombin to thrombin → Thrombin will convert fibrinogen to fibrin.

  - **Fibrin** enmesh platelets, blood cells and plasma and aid in the stabilization of the primary platelet plug and the formation of blood clot.
  - **Vitamin K is needed for the production of**: prothrombin, factors VII, IX, X and protein C.
  - **Calcium** is needed in all reactions of the intrinsic pathway except the first 2 steps (formation of factor XIIa and formation of factor Xia).
- **Fibrinolysis:**
  - Plasminogen → plasmin → breaking fibrin
  - Conversion of plasminogen to plasmin is stimulated by tissue plasminogen activator (TPA) & urokinase.
  - Plasmin formation is inhibited by plasmin inhibitor.
- **Intravascular anticoagulants:**
  - Smoothness of the endothelium
  - A layer of glycocalyx in the endothelium
  - Thrombomodulin (protein bound to endothelium): binding thrombin to form thrombomodulin-thrombin complex and activating protein C. protein C in turn will inactivate factors V & VIII.
  - Antithrombin III inactivated thrombin.
  - Heparin: produced by mast cells and basophils and aids in the removal of thrombin from the circulation.