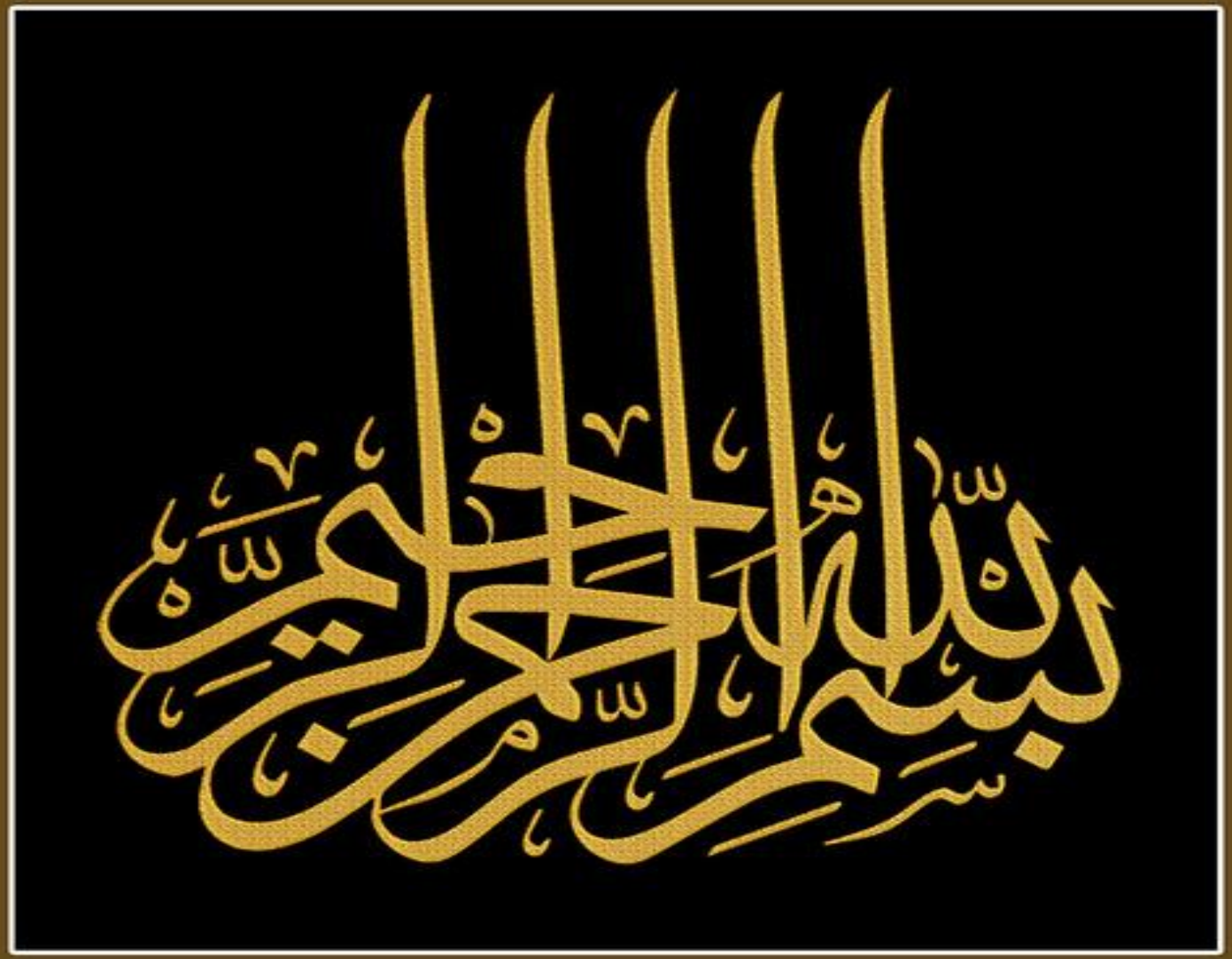

بسم الله الرحمن الرحيم

# Platelets, Blood Clotting and Coagulation

Dr. Taj

# Platelets


Thrombocytes are

- Fragments of megakaryocytes in bone marrow. The average life span of circulating platelets is 8 to 10 days

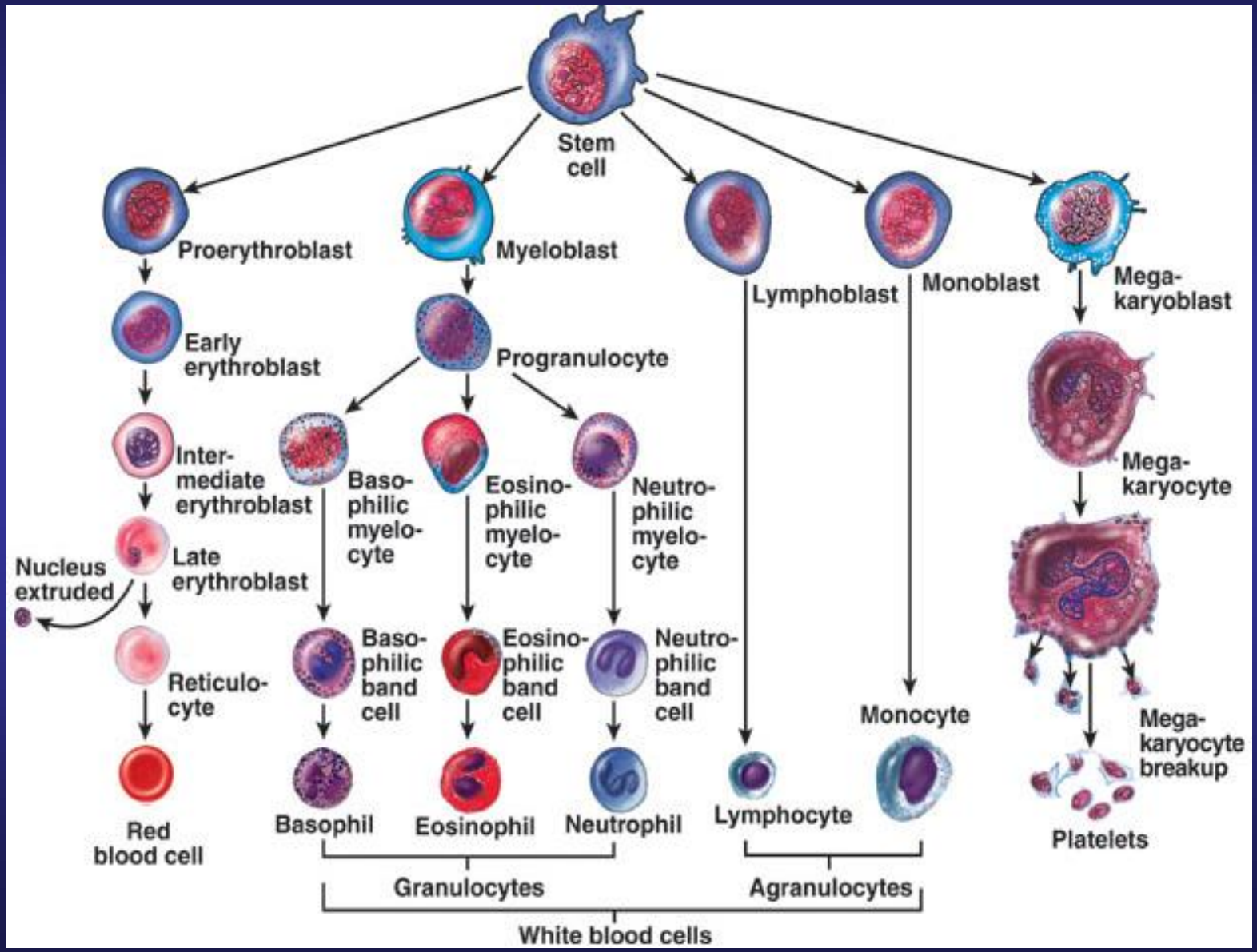
# What is Thrombopoiesis

- Thrombopoiesis is the process of thrombocyte generation. Thrombocytes are ligations of the cytoplasm from megakaryocytes. A single megakaryocyte can give rise to thousands of thrombocytes.

# What stimulates Thrombopoiesis

Thrombopoietin is a glycoprotein hormone produced by the liver and kidney which regulates the production of platelets. It stimulates the production and differentiation of megakaryocytes, the bone marrow cells that bud off large numbers of platelets.

# Hematopoiesis



# Platelets – cont.

Site of formation: Bone marrow

Steps:

Stem cell

Megakaryoblast

Megakaryocyte

Platelets

# Platelets Formation (Thrombopoiesis)

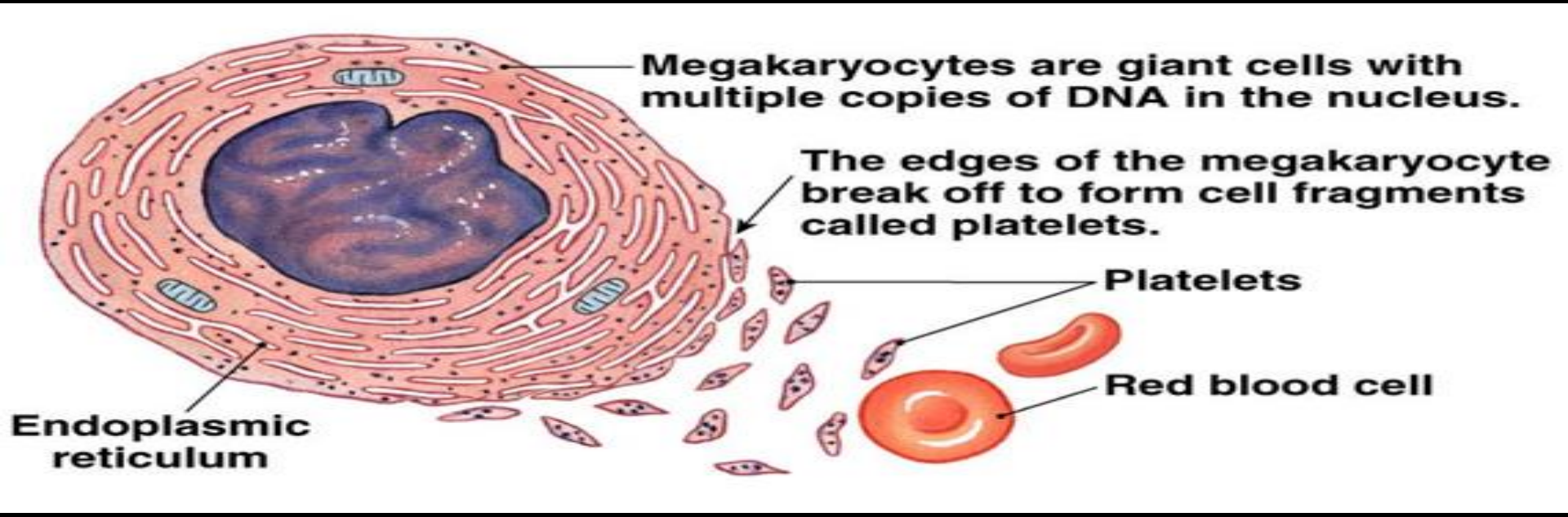
## Regulation of thrombopoiesis by Thrombombopoietin

# Platelet Production

As megakaryocytes develop into giant cells, they undergo a process of fragmentation that results in the release of over 1,000 platelets per megakaryocyte. This is mainly controlled by a hormone. The dominant hormone controlling megakaryocyte development is ***THROMBOPOIETIN***

# Platelets

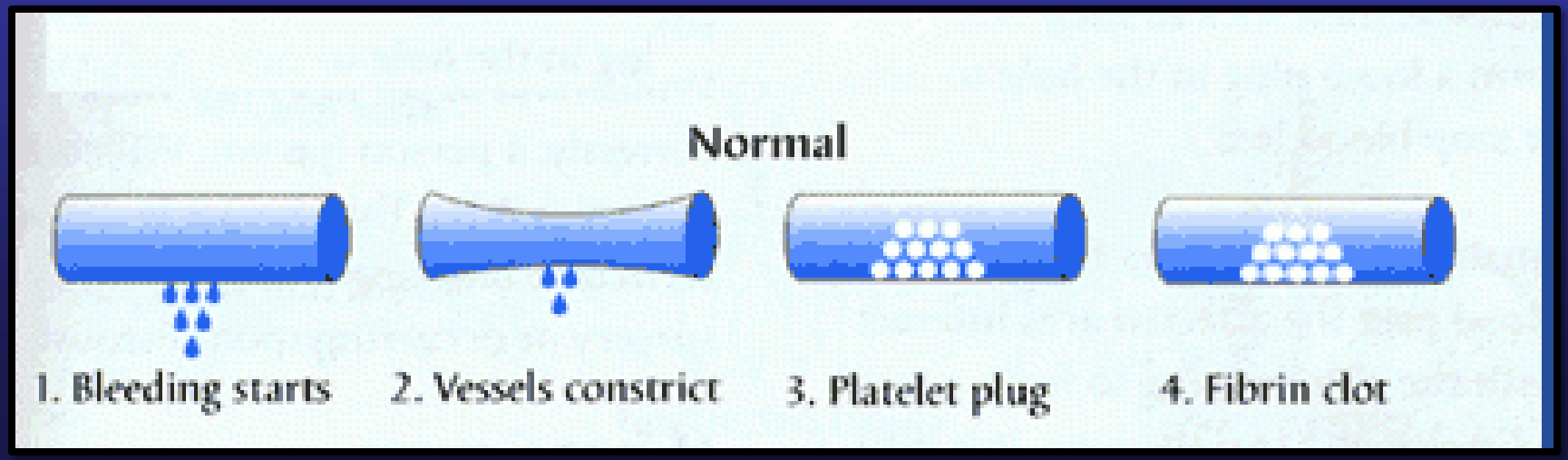
- Platelets are non-nucleated, small, round or oval discs.
- They are formed in the bone marrow by fragmentation of the cytoplasm of giant cells called "***Megakaryocytes***".
- Platelet count normally = 150,000-400,000/µl.



# Function of Platelets

- Plays a role in ***Hemostasis*** = prevention of blood loss.

- Whenever a vessel is severed or ruptured, Hemostasis is achieved by several mechanisms;
  1. Vascular spasm.
  2. Formation of a platelet plug.
  3. Formation of a blood clot as a result of blood coagulation.



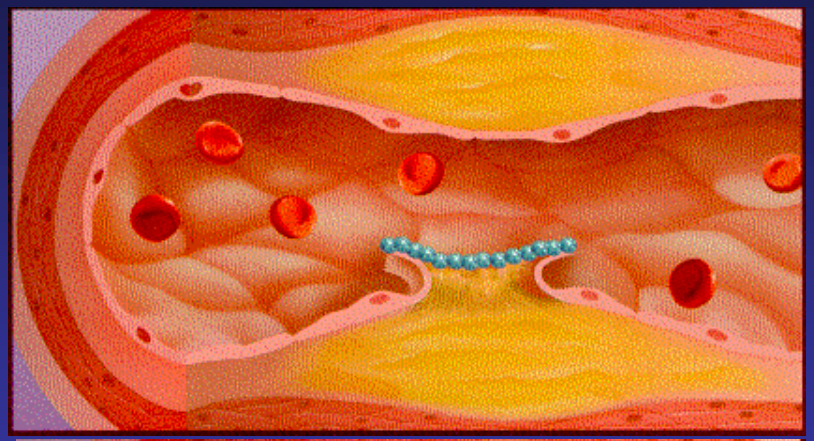
# Platelet Functions

Begins with Platelet activation

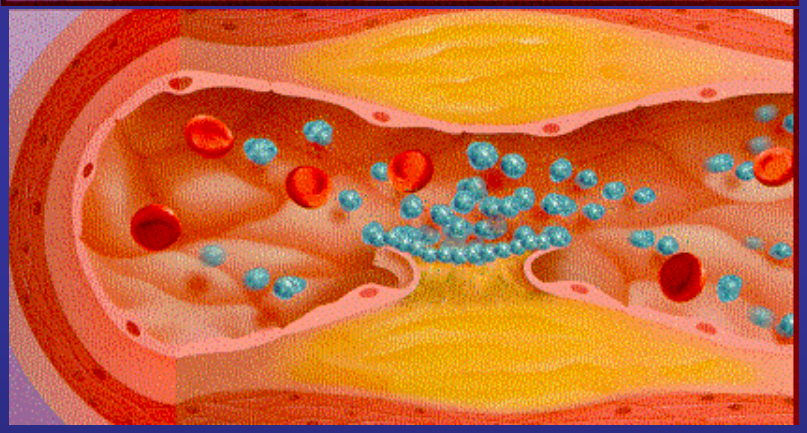
# Platelet Activation

- Adhesion
- Shape change
- Aggregation
- Release
- Clot Retraction

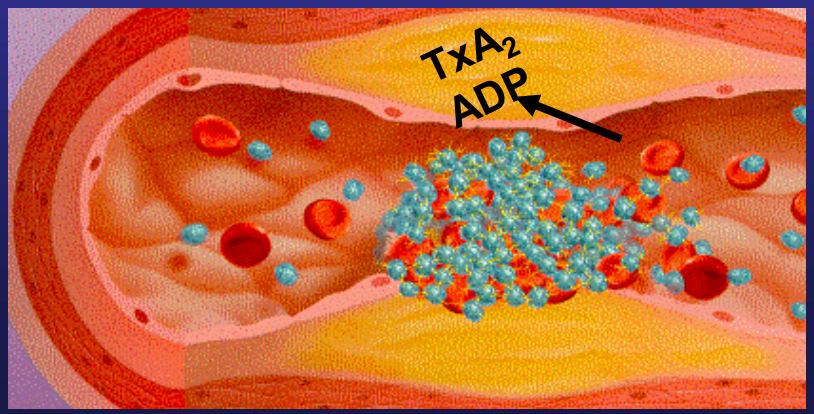
# Platelet function



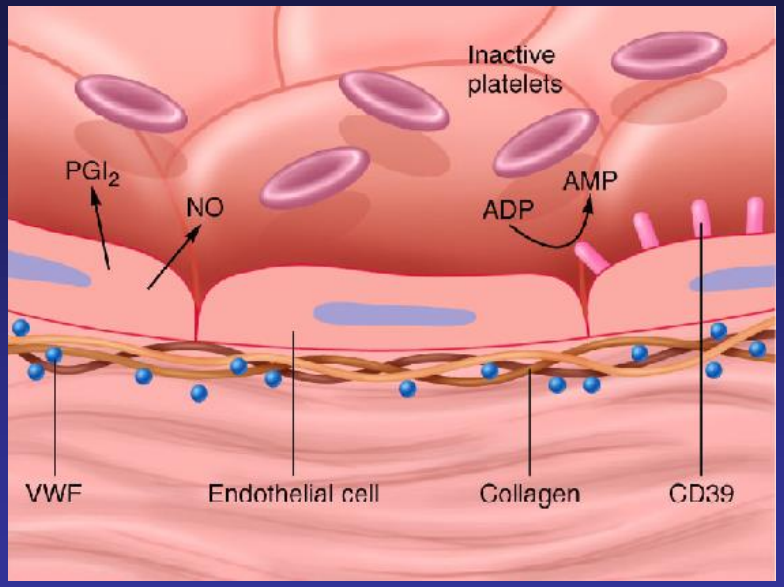
Adhesion

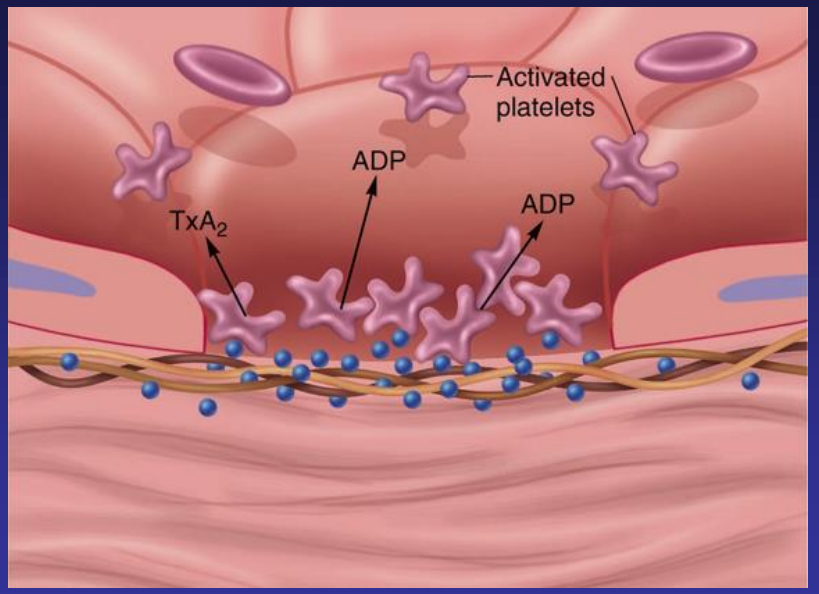


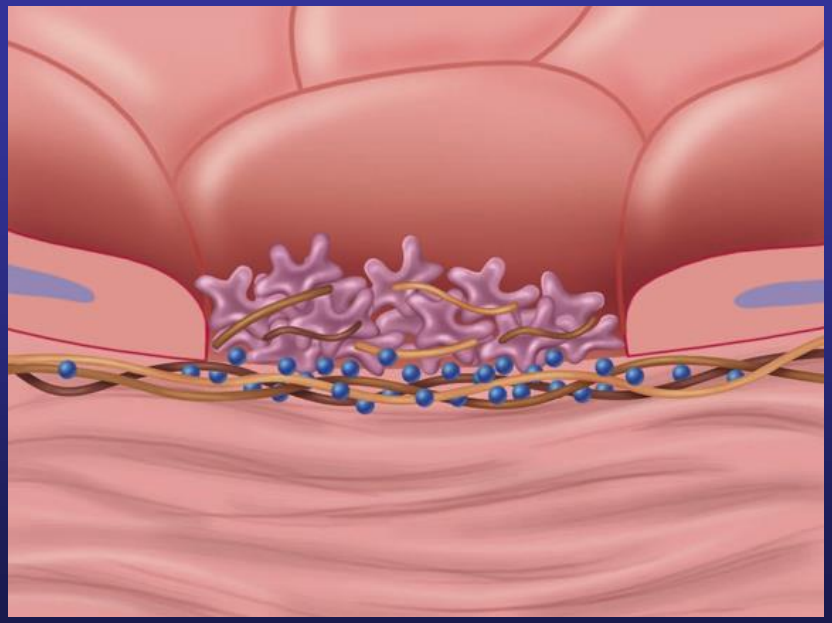
Aggregation




Secretion

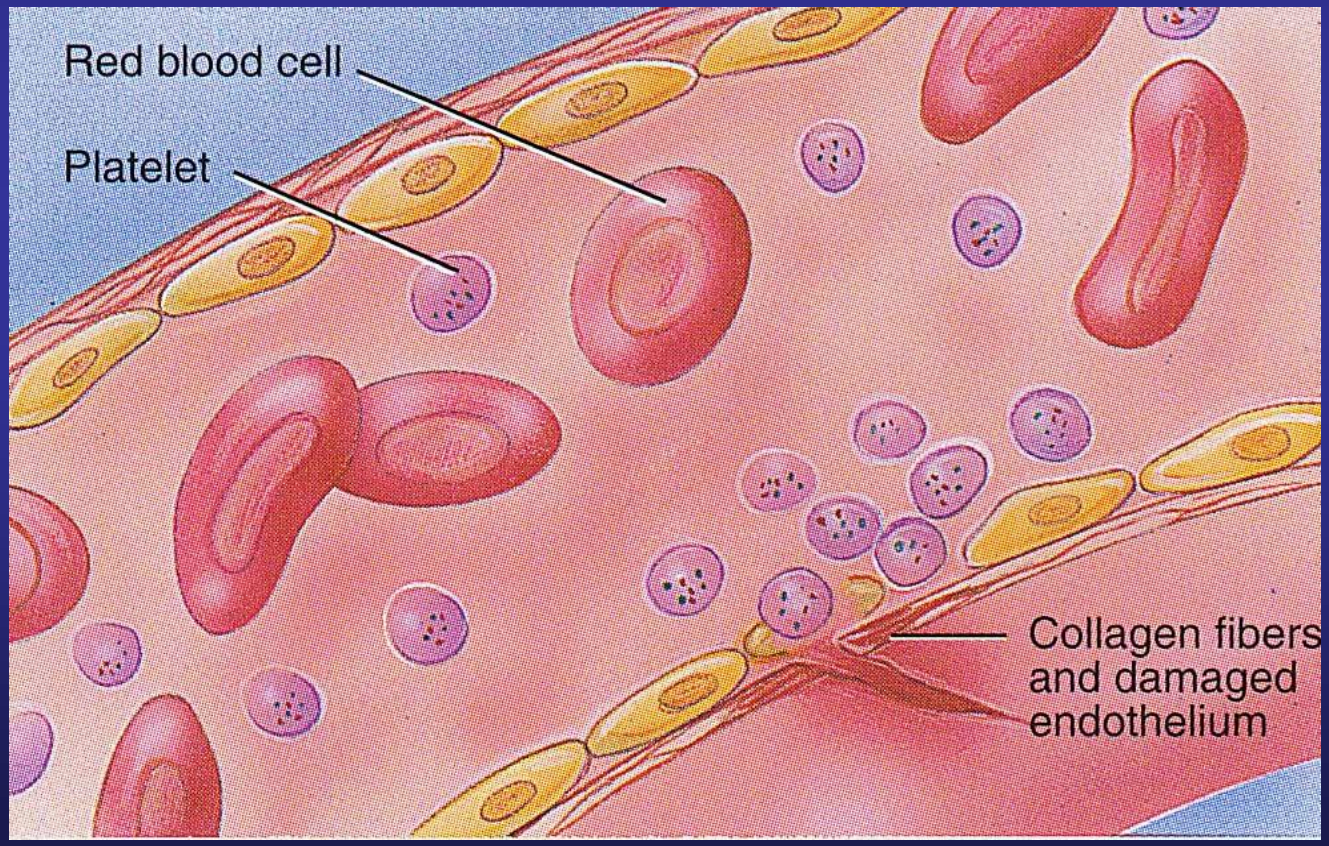

Inactive platelets
$PGI_2$
NO
ADP
AMP
VWF
Endothelial cell
Collagen
CD39


Activated platelets
ADP
ADP
$TxA_2$



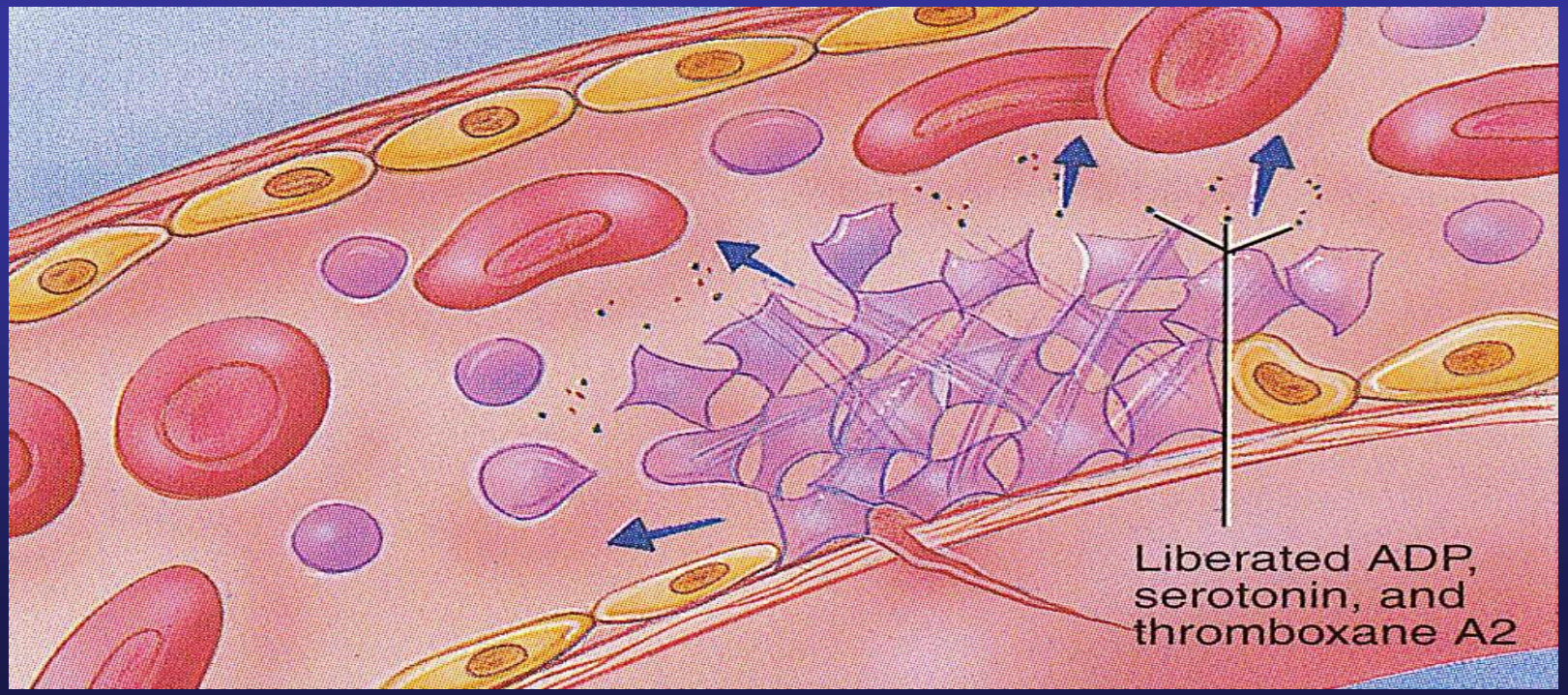
# Platelet Adhesion

Platelets stick to exposed collagen underlying damaged endothelial cells in vessel wall



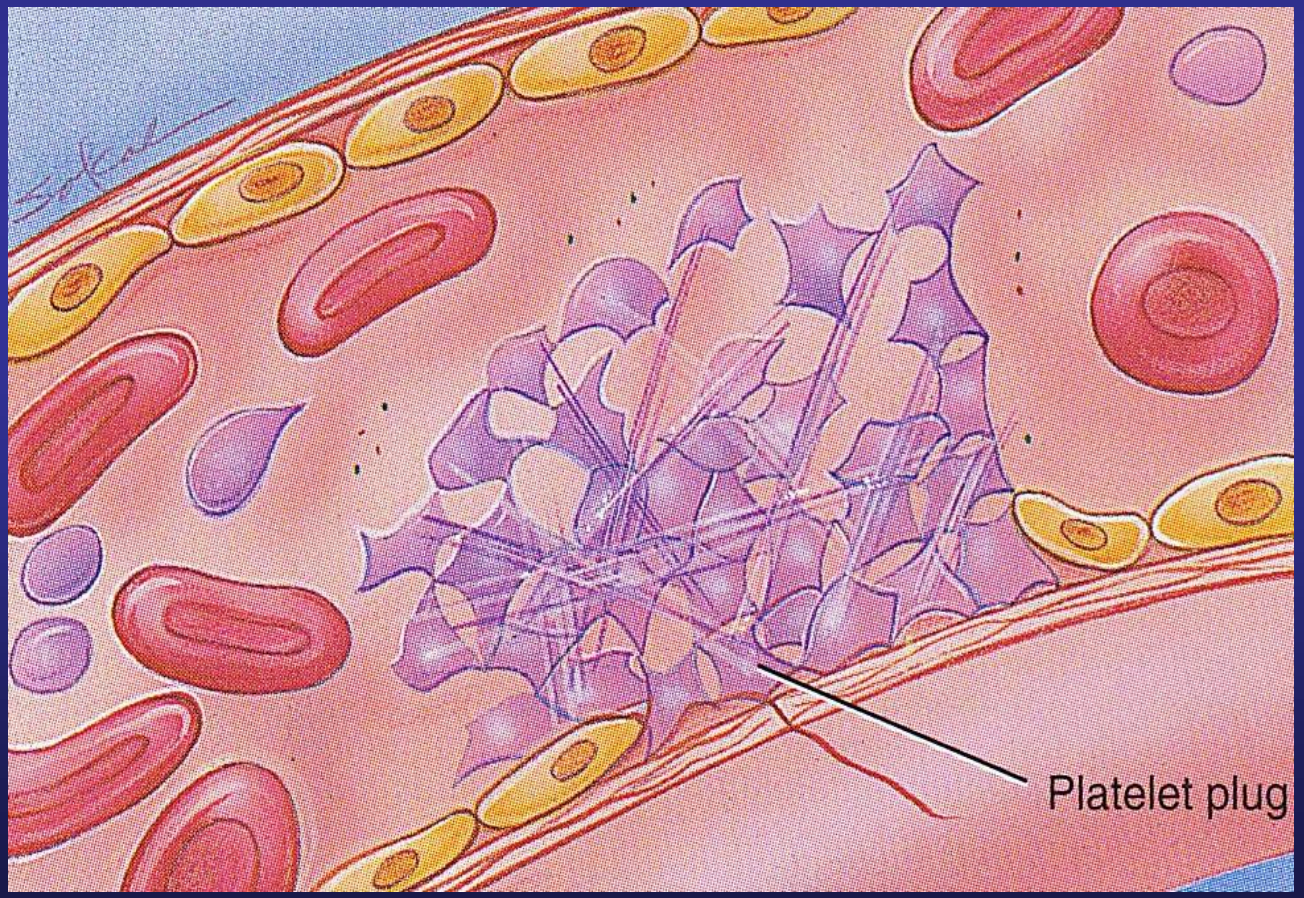
# Platelet Release Reaction

- **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**

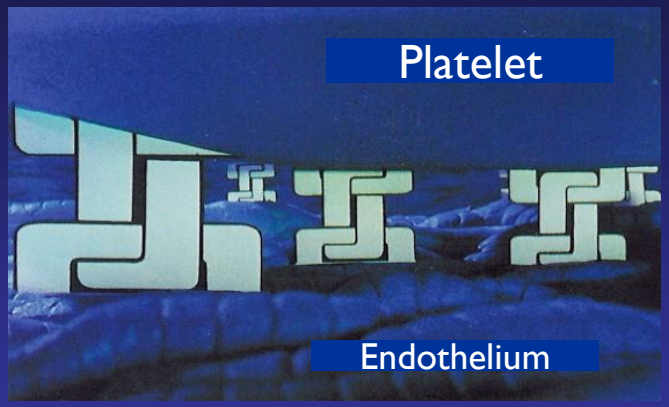


# Platelet Aggregation

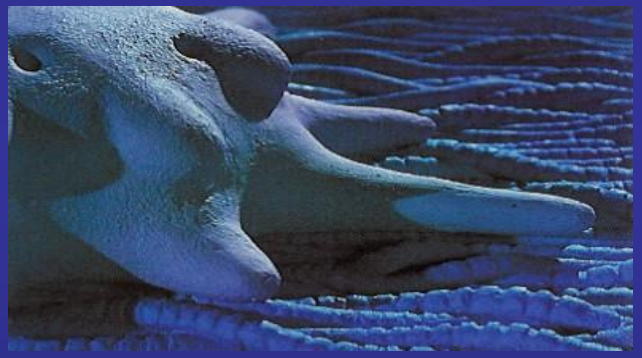
- **Activated platelets stick together and activate new platelets to form a mass called a <u>Platelet Plug</u>**
- ***<u>Plug is reinforced by fibrin threads formed during clotting process</u>***



1. Adhesion

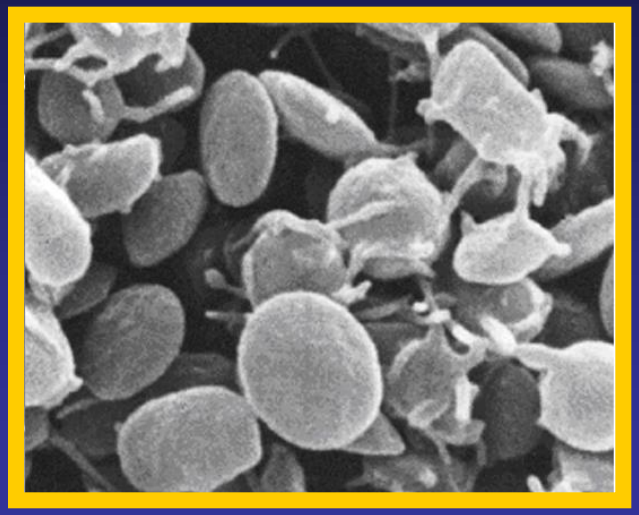



2. Shape change

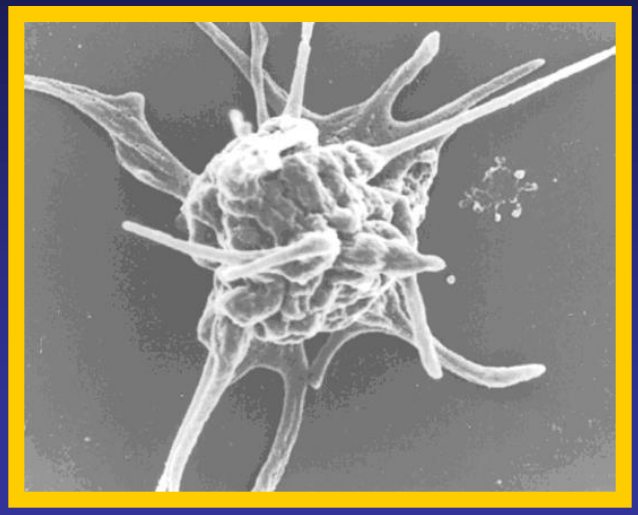


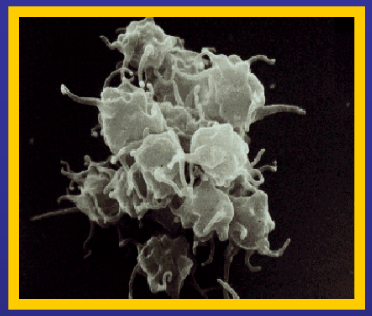
3. Aggregation

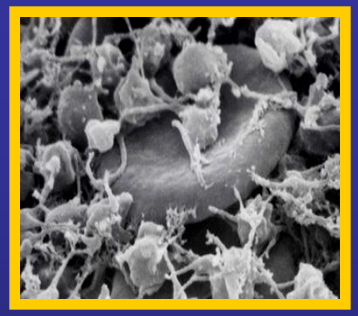
## Resting platelet

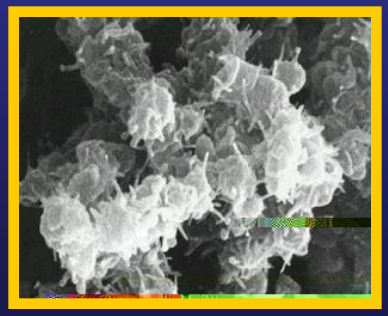


## Activated platelet







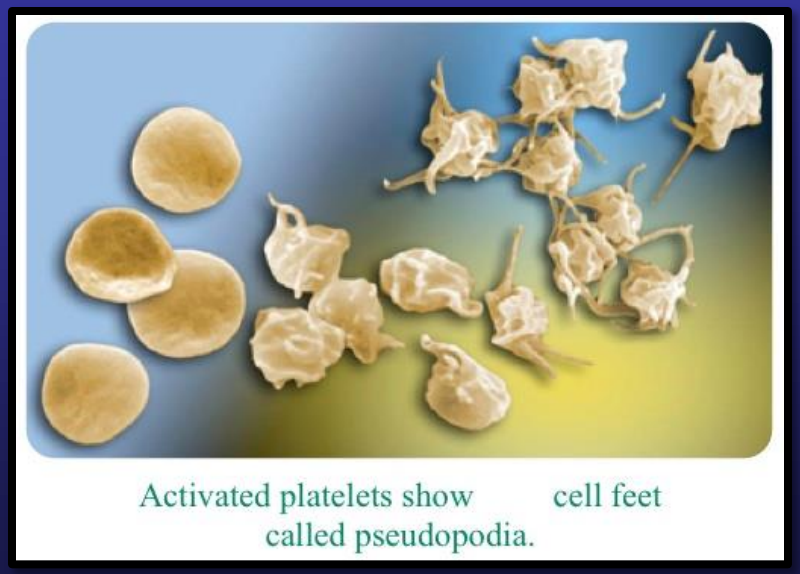


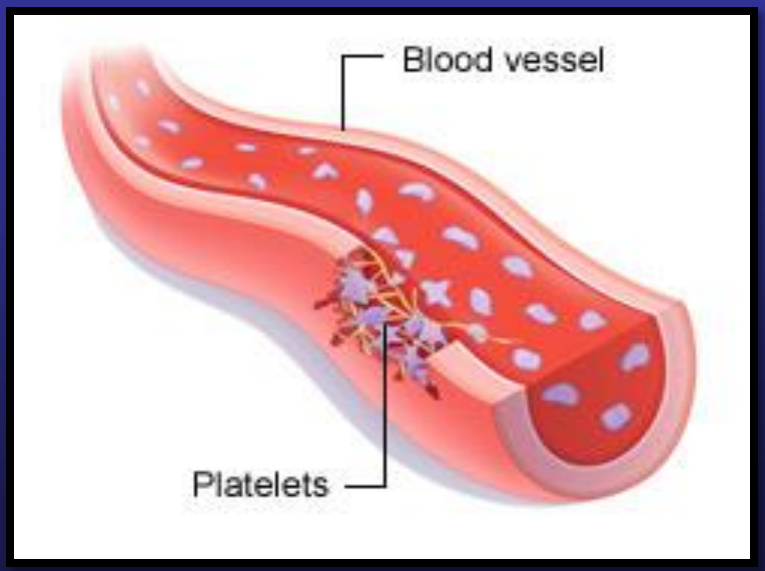
# Platelet shape change and Aggregation

# Platelet Aggregation

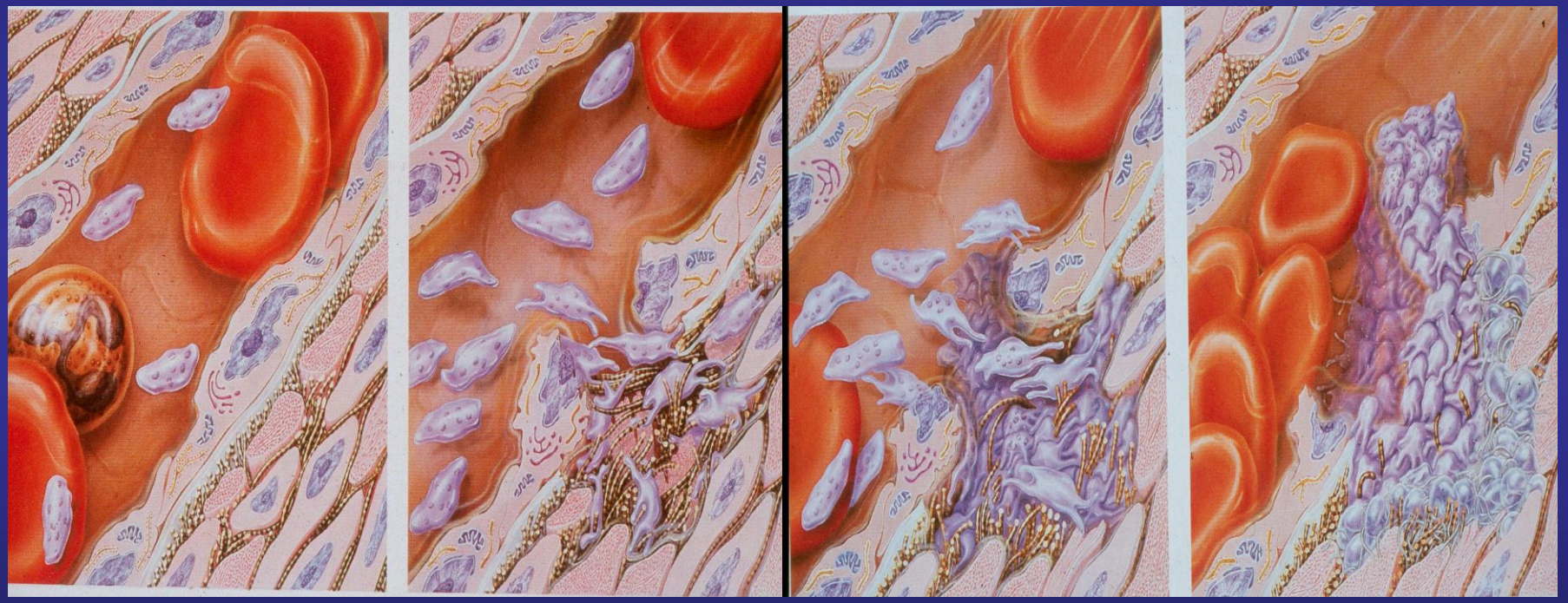
# Platelet Plug Formation

1. Blood vessel injury.
2. Platelets come in contact with damaged blood vessel.
3. They become activated and adhere to the injured area.
4. This will activate even more platelets to come to the injured area resulting in platelet plug formation.



# Platelet haemostatic plug formation



# Platelet Plug formation Cont...

- The platelet plug is a loose plug that is usually successful in blocking the blood loss if the vascular opening is small.

- Then, during the process of blood coagulation, the stronger fibrin threads are formed that will strengthen the platelet plug.

# Platelet Plug

Aggregation of platelets at the site of injury to stop bleeding

- Exposed collagen attracts platelets
- Thus these Activated platelets release ADP & TXA2 → ↑ the stickiness of platelets → ↑ Platelets aggregation → plugging of the cut vessel

==========x==========x==========

- Intact endothelium secret prostacyclin → inhibit aggregation

# Activated Platelets

Secrete:

1. Serotonin or 5-hydroxytryptamine (5HT) → vasoconstriction
2. Platelet phospholipid is a platelet derived clotting factor (PF3) → clot formation
3. Thromboxane A2 (TXA2) is a prostaglandin formed from archidonic acid.

   Function:

   - vasoconstriction
   - Platelet aggregation

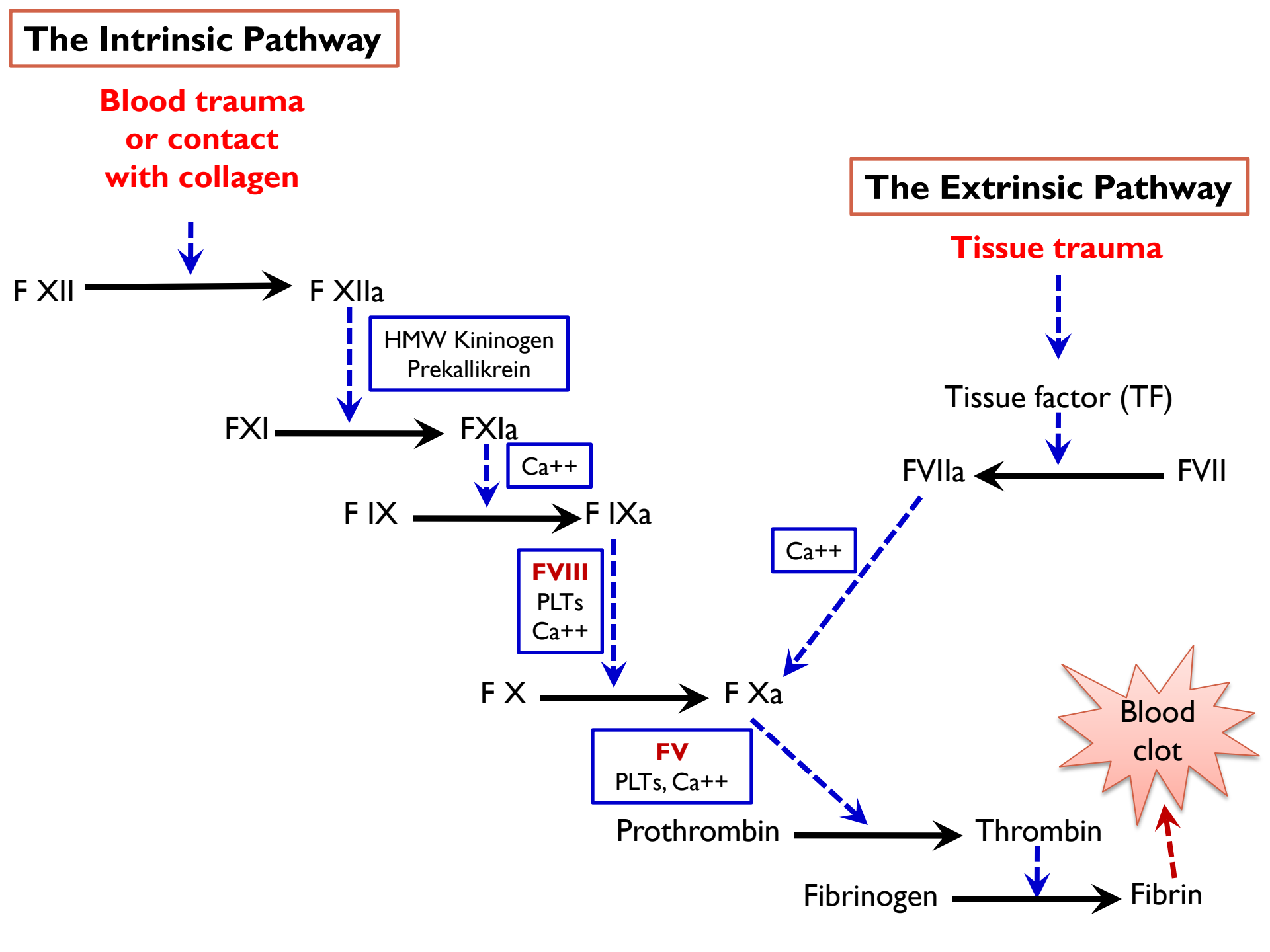
(TXA2 inhibited by ASPIRIN)

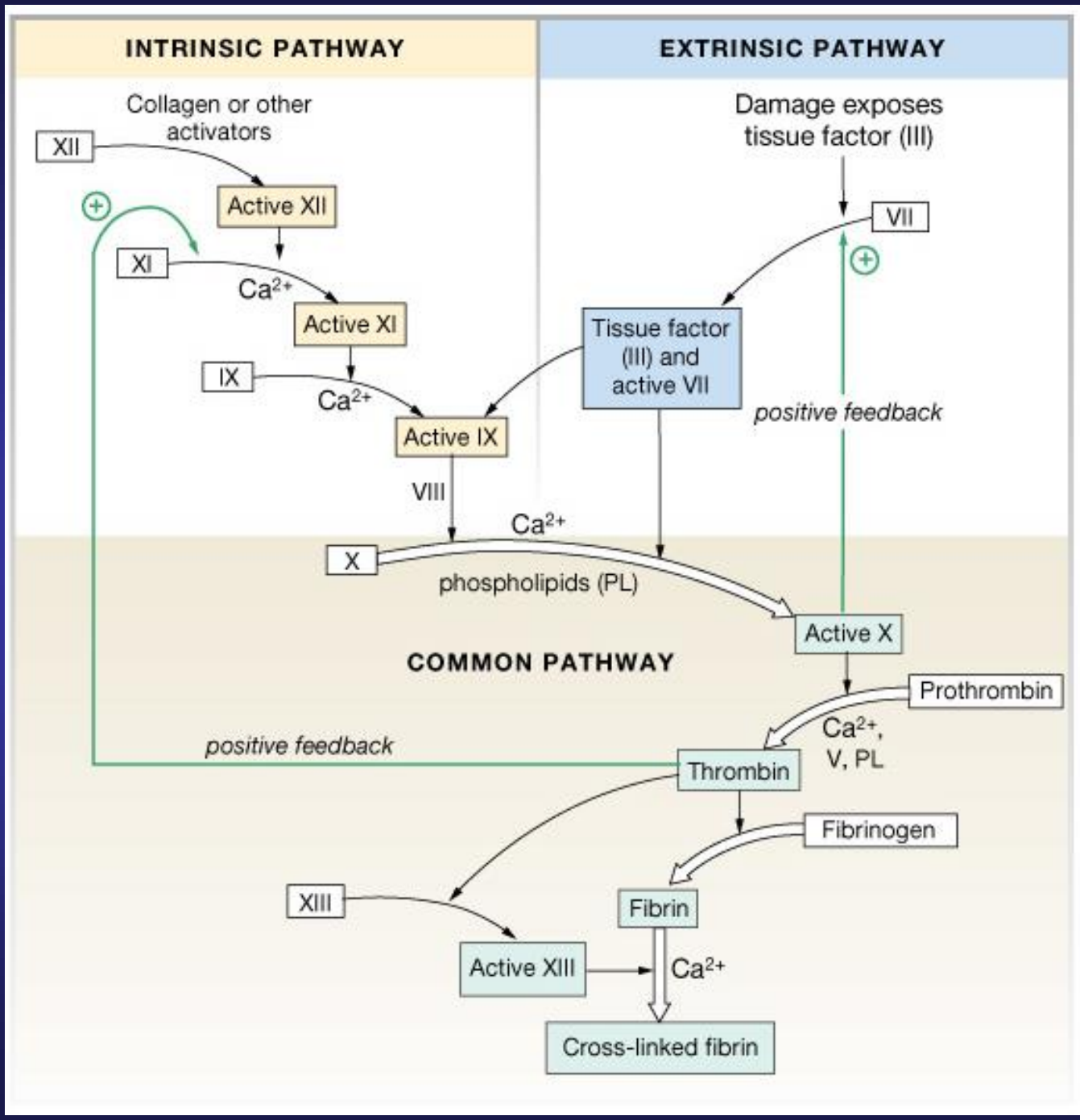
# Blood coagulation

- Initiation on blood coagulation occurs by two ways:

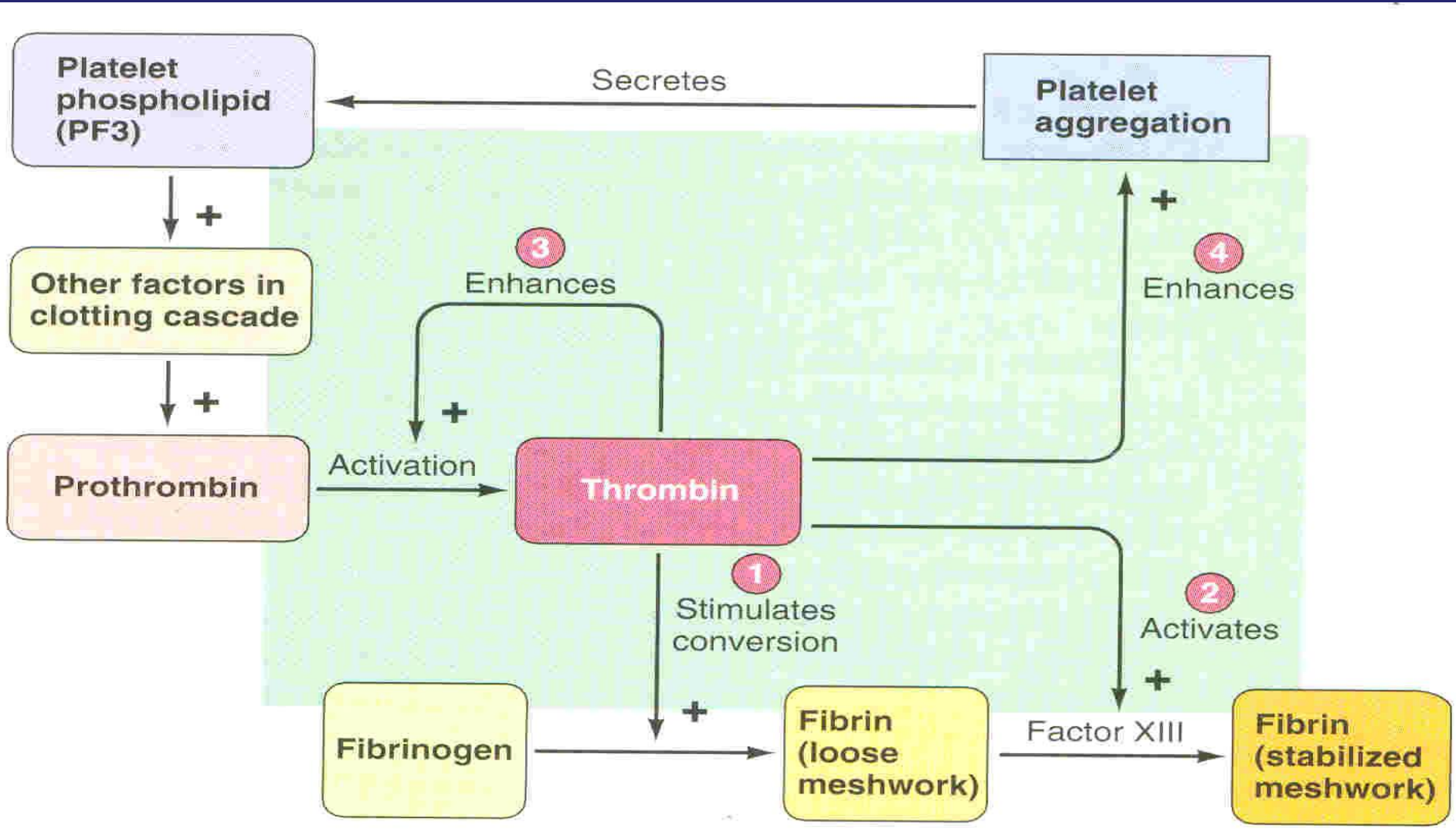
1. ***The extrinsic pathway***: initiated by trauma to blood vessel.

2. ***The intrinsic pathway***: initiated in the blood itself.


The Intrinsic Pathway
Blood trauma or contact with collagen
F XII
F XIIa
HMW Kininogen
Prekallikrein
FXI
FXIa
Ca++
F IX
F IXa
FVIII
PLTs
Ca++
F X
F Xa
FV
PLTs, Ca++
Prothrombin
Thrombin
Fibrinogen
Fibrin
The Extrinsic Pathway
Tissue trauma
Tissue factor (TF)
FVIIa
FVII
Ca++
Blood clot


INTRINSIC PATHWAY
EXTRINSIC PATHWAY
Collagen or other activators
XII
Active XII
XI
Ca2+
Active XI
IX
Ca2+
Active IX
VIII
Damage exposes tissue factor (III)
VII
Tissue factor (III) and active VII
positive feedback
Ca2+
X
phospholipids (PL)
Active X
COMMON PATHWAY
Prothrombin
Ca2+, V, PL
positive feedback
Thrombin
Fibrinogen
XIII
Fibrin
Active XIII
Ca2+
Cross-linked fibrin

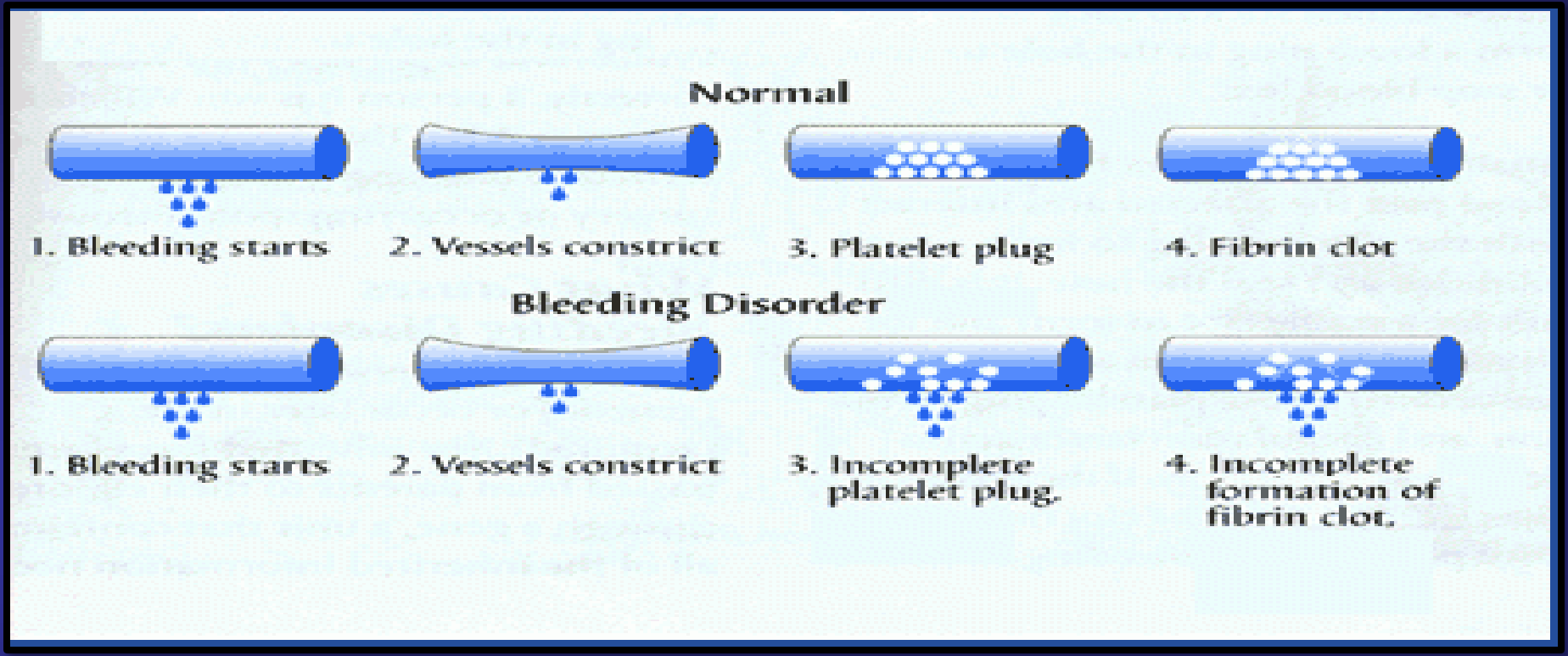
# ROLE OF THROMBIN IN HEMOSTASIS



# ROLE OF CALCIUM IONS IN CLOTTING

- No $Ca^{++} \rightarrow$ No Clotting
- Blood samples are prevented from clotting by adding:
  - Citrate ions $\rightarrow$ Deionization of $Ca^{++}$
  - Oxalate ions $\rightarrow$ ppt the $Ca^{++}$

# Bleeding Disorders




- Excessive bleeding can result from;
  - Platelet defects: deficiency in number (thrombocytopenia) or defect in function.
  - Deficiency in coagulation factors (e.g. hemophilia).
  - Vitamin K deficiency.

# BLEEDING & CLOTTING DISORDERS

A. **Liver diseases & Vitamin-K deficiency**
B. **Hemophilia**
C. **Thrombocytopenia**

# BLEEDING DISORDERS

## Liver diseases & Vitamin-K deficiency

- e.g. Hepatitis, Cirrhosis
  - Decreased formation of clotting factors
  - Increased clotting time

- Vitamin K dependent factors
  - **Prothrombin**, Factor **VII, IX, X**

# HEMOPHILIA

- **HEMOPHILIA - A**
  - Classic Hemophilia
  - 85 % cases
  - Def. Of factor VIII
- **HEMOPHILIA - B**
  - 15 % cases
  - Def. Of factor IX

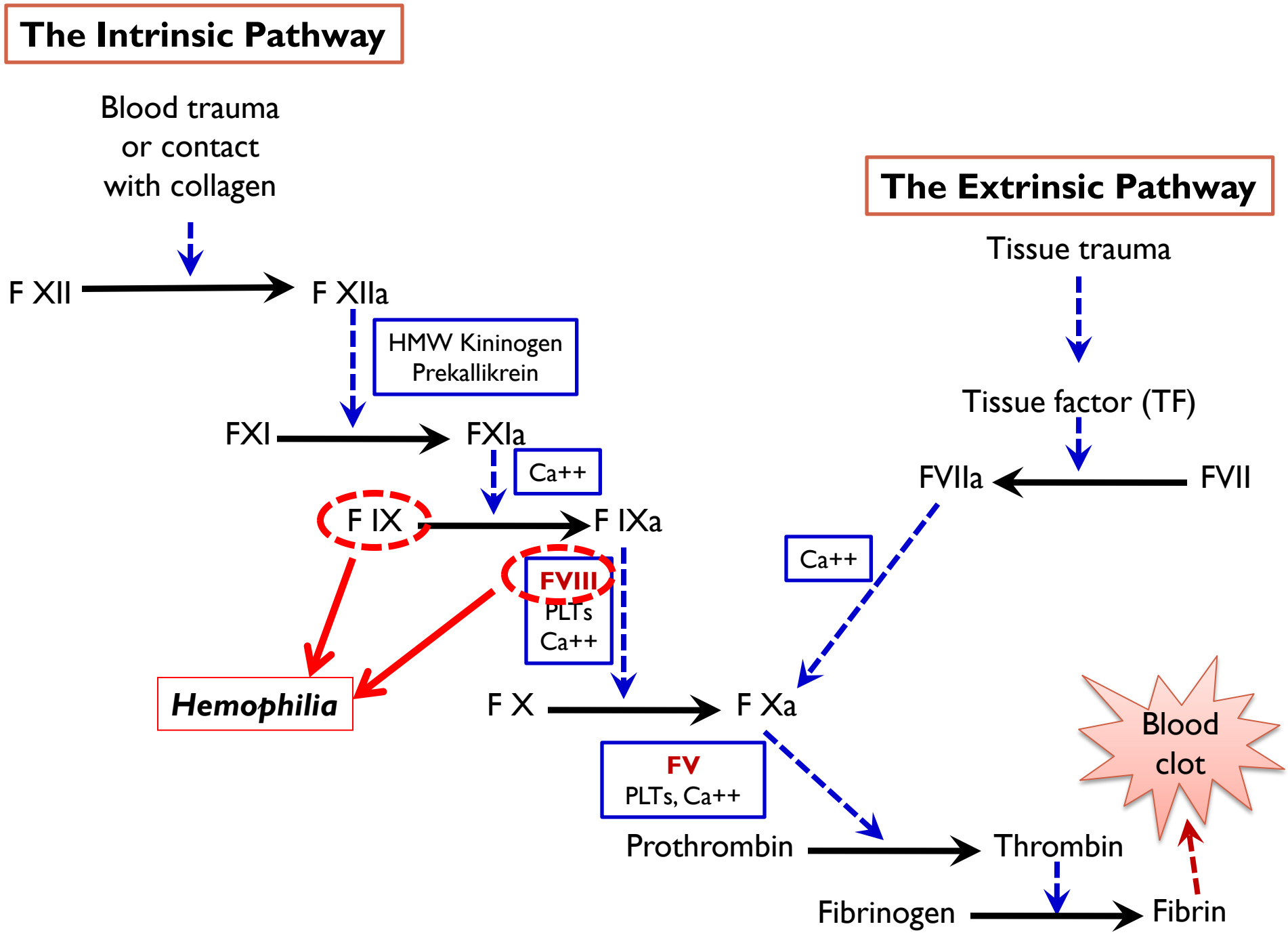
# HEMOPHILIA

- Genetic disorders
- Transmitted by female chromosome as recessive trait, it is X linked.
- Occurs exclusively in male. Females are carriers.

- Types
  - Hemophilia A
  - Hemophilia B

# HEMOPHILIA

- **Clinical Features**
  - **Easy bruising, massive bleeding after trauma or operation, hemorrhages in joints**
  - **Deficiency of Factor VIII ---- Hemophilia A**
  - **Deficiency of Factors IX ---- Hemophilia B**
  - **Rx**
    - **Injection of factor VIII (Hemophilia A)**
    - **Injection of factor IX (Hemophilia B)**


The Intrinsic Pathway
Blood trauma
or contact
with collagen
F XII
F XIIa
HMW Kininogen
Prekallikrein
FXI
FXIa
Ca++
F IX
F IXa
FVIII
PLTs
Ca++
Hemophilia
F X
F Xa
The Extrinsic Pathway
Tissue trauma
Tissue factor (TF)
FVIIa
FVII
Ca++
FV
PLTs, Ca++
Prothrombin
Thrombin
Fibrinogen
Fibrin
Blood
clot

# THROMBOCYTOPENIA

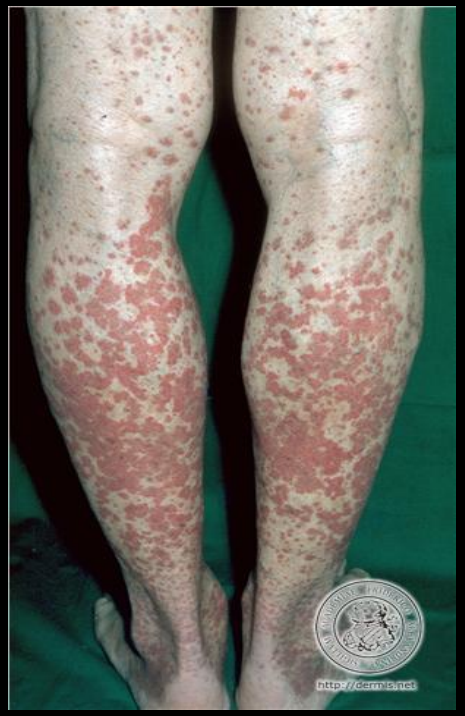
- PLT count upto 50,000 ul
- Less than 10,000 ------ Fatal
- ETIOLOGY
- Decreased production
  - Aplastic anemia
  - Leukemia
  - Drugs
  - Infections (HIV, Measles)

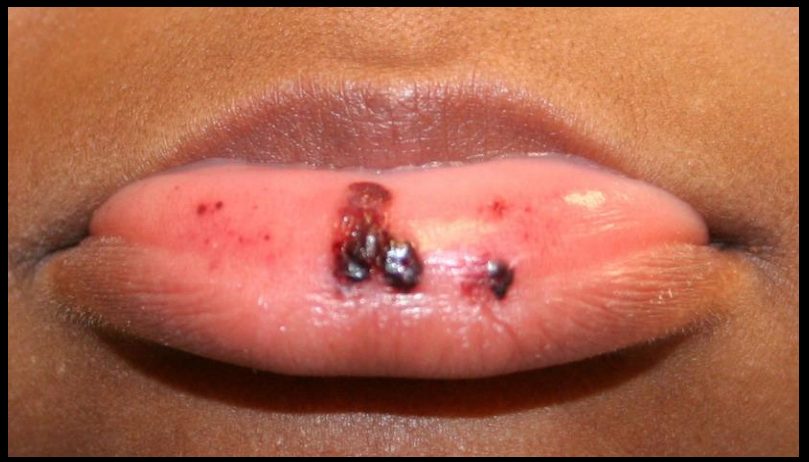
# THROMBOCYTOPENIA

- Increased destruction
  - ITP
  - Drugs
  - Infections
- Clinical Features
  - Easy brusability
  - Epistaxis
  - Gum bleeding
  - Hemorrhage after minor trauma
  - Petechiae/Ecchumosis

# THROMBOCYTOPENIA

- Diagnosis
  - PLT decreased
  - B.T increased
- Rx
  - Rx of the underlying cause
  - PLT concentrates
  - Fresh whole blood transfusion
  - Splenectomy





# Bleeding Disorders Cont…

- Hemophilia:
  - ↑ bleeding tendency.
  - X-linked disease.
  - Affects males.
  - 85% due to FVIII deficiency (hemophilia A), and 15% due to FIX deficiency (hemophilia B).

- Vitamin K deficiency & liver disease:
  - Almost all coagulation factors are synthesized in the liver.
  - Prothrombin, FVII, FIX, & FX require vitamin K for their synthesis.

# CLINICAL NOTE

The **VWF** has a dual role in hemostasis:

***first*** it *promotes platelet adhesion* to thrombogenic surfaces as well as platelet-to-platelet cohesion during thrombus formation;

***second*** it is the *carrier for FVIII in plasma*. FVIII acts as a co-factor to accelerate the activation of factor X by activated factor IX in the coagulation cascade.

# Anticoagulants

- Heparin
  - Liver, lungs, mast cells, basophils
  - Direct antithrombin
  - Prevent the conversion of Prothrombin to Thrombin
  - Injection only
  - 6-8 hours

- Warfarin
  - Almost all coagulation factors are synthesized in the liver.
  - Suppresses the synthesis of Prothrombin, FVII, FIX, & FX vitamin K dependent factors
  - Orally
  - 48 hours

*Thank you*