LECTURE 11

Hemostasis

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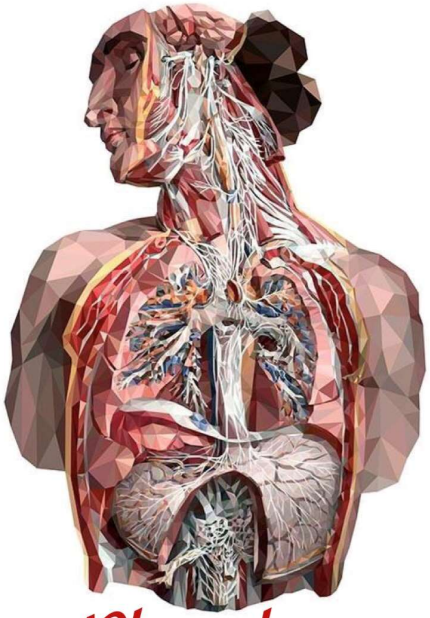
- Red : important
- Black : in male / female slides
- Pink : in girls slides only
- Blue : in male slides only
- Green : notes, Extra

Reviewed by Razan AlRabah & Khalid Alkhani



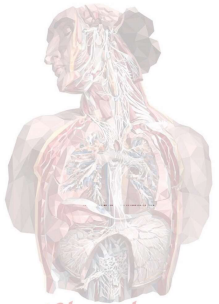
Physiology

Team 438

KSU

Objectives:-

- Recognize different stages of hemostasis.
- Describe formation and development .
- Describe the role of platelets in hemostasis.
- Recognize different clotting factors.
- Describe the cascade of clotting.
- Describe the cascade of intrinsic pathway.
- Describe the cascade of extrinsic pathways.
- Recognize the role of thrombin in coagulation.
- Recognize process of fibrinolysis and function of plasmin.



It is **Haemostasis or Hemostasis**

Not Homeostasis : The ability to maintain a constant internal environment in response to environmental changes

Definition:

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

1-Objective: Recognize different stages of hemostasis

Mechanisms:

1. Vessel wall
2. Platelet
3. Blood coagulation
4. Fibrinolytic system

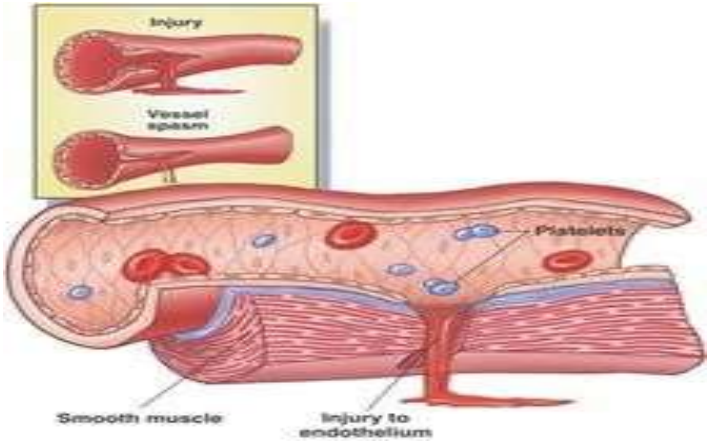
Hemostatic Mechanisms

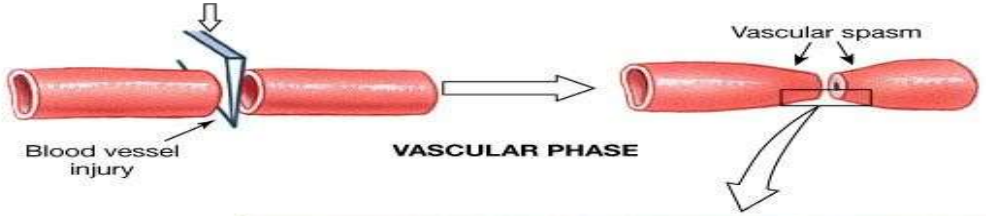
- **1.<u>Vessel wall</u>**

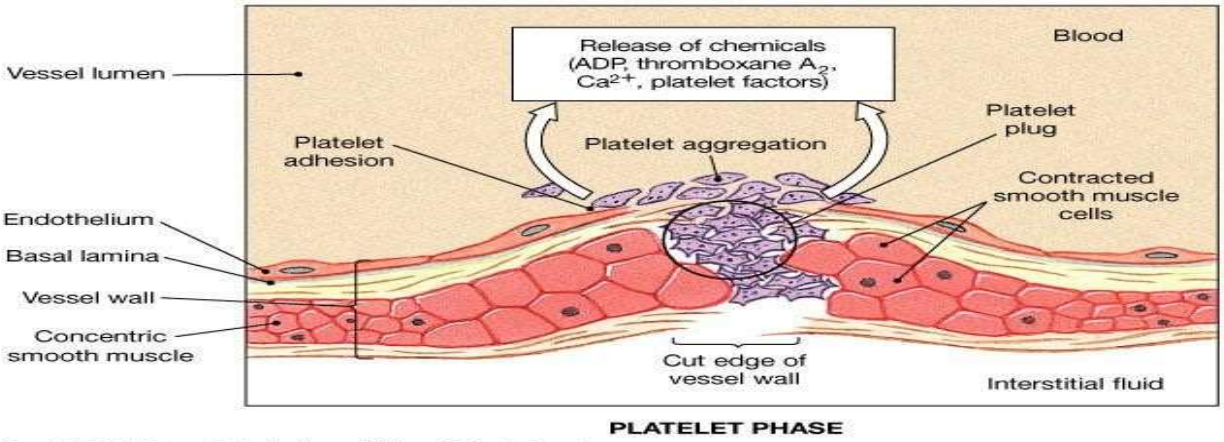
- Immediately After injury a localized Vasoconstriction.

- Mechanism:

- **<u>Systemic</u>** release of adrenaline
- Nervous factors
- **<u>local</u>** release of thromboxane A2 & 5HT(5hydroxytryptamine) by platelets
- Myogenic spasm
- Nervous factors
- Humoral factors







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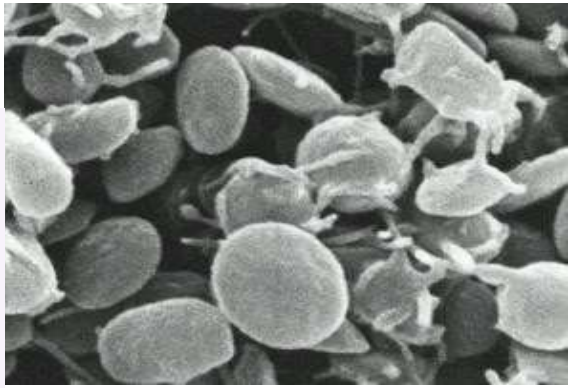
Platelets (Thrombocytes)

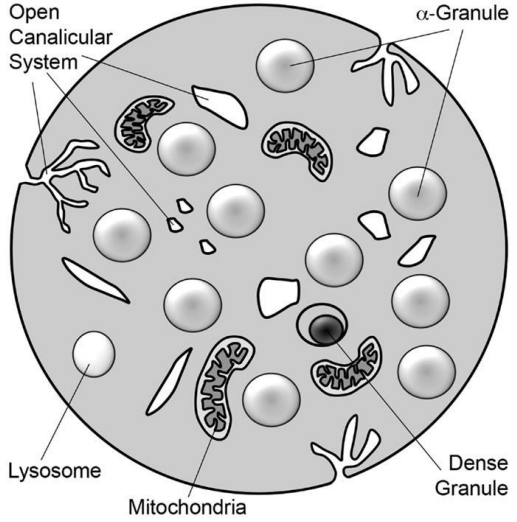
2-objective: Describe formation and development of platelet.

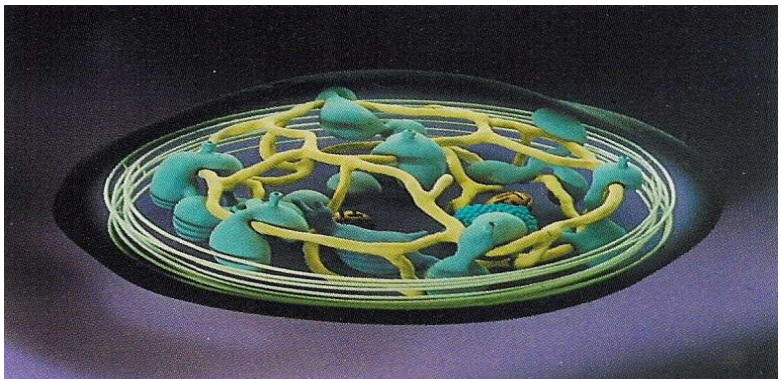


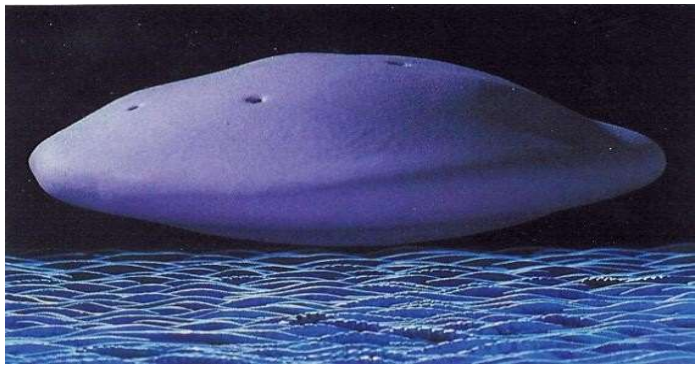
- small <u>disc shaped</u> cells

- Platelet count = $150x10^3$-$300x10^3$/ml,

- life span 8-12 days
- Contain high calcium content & rich in ADP
- Active cells contain contractile protein





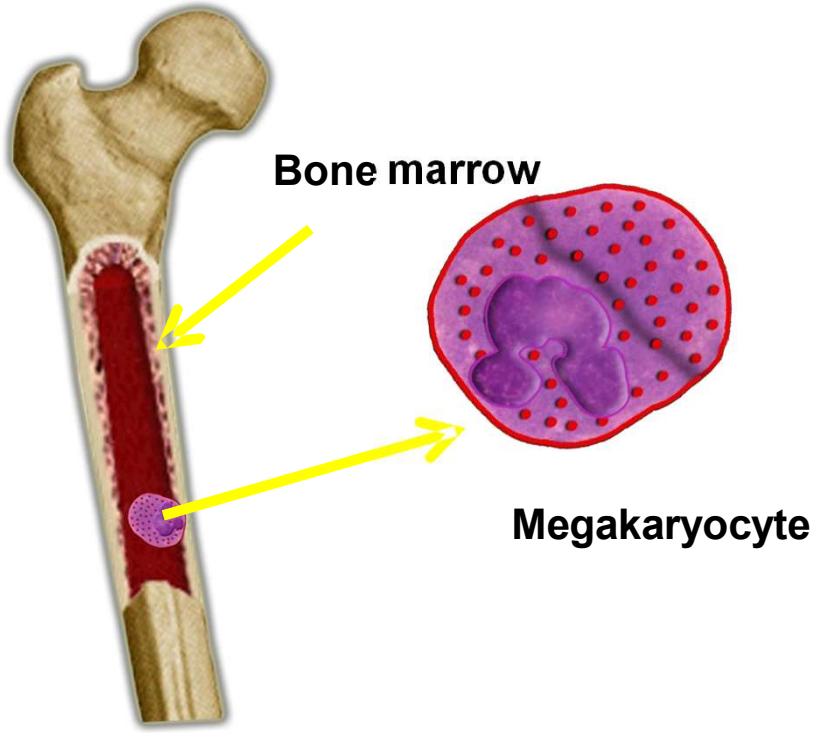


Platelets - cont

تسمى بالخلية الام لانها اذا تجزأت لأجزاء متساوية راح تعطينا platelets
All the structures of platelets are the same

- Thrombocytes
- Are Fragments of megakaryocytes in the bone marrow

- Regulation of thrombopoiesis By:
- Thrombombopoietin
- (Released from liver)



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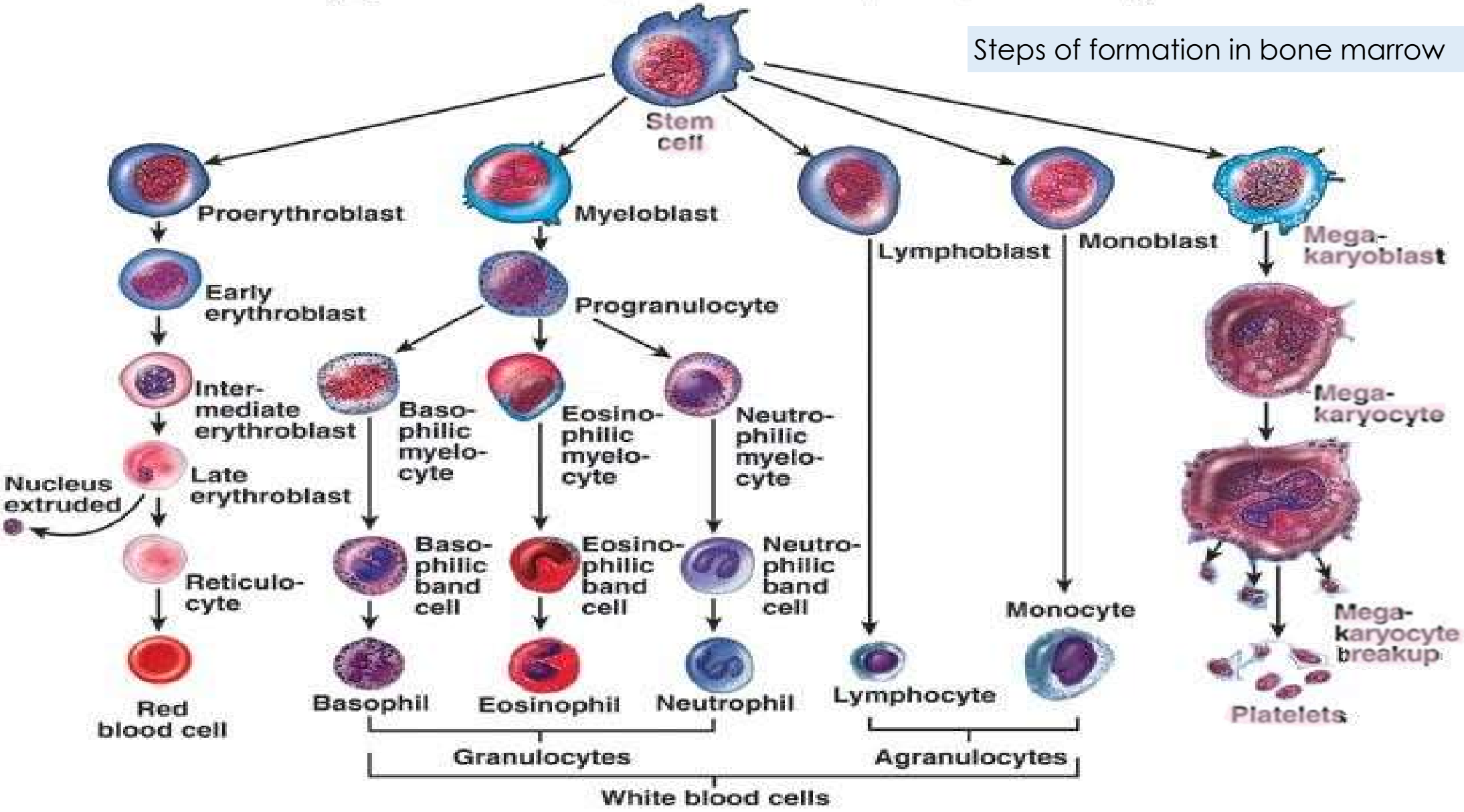
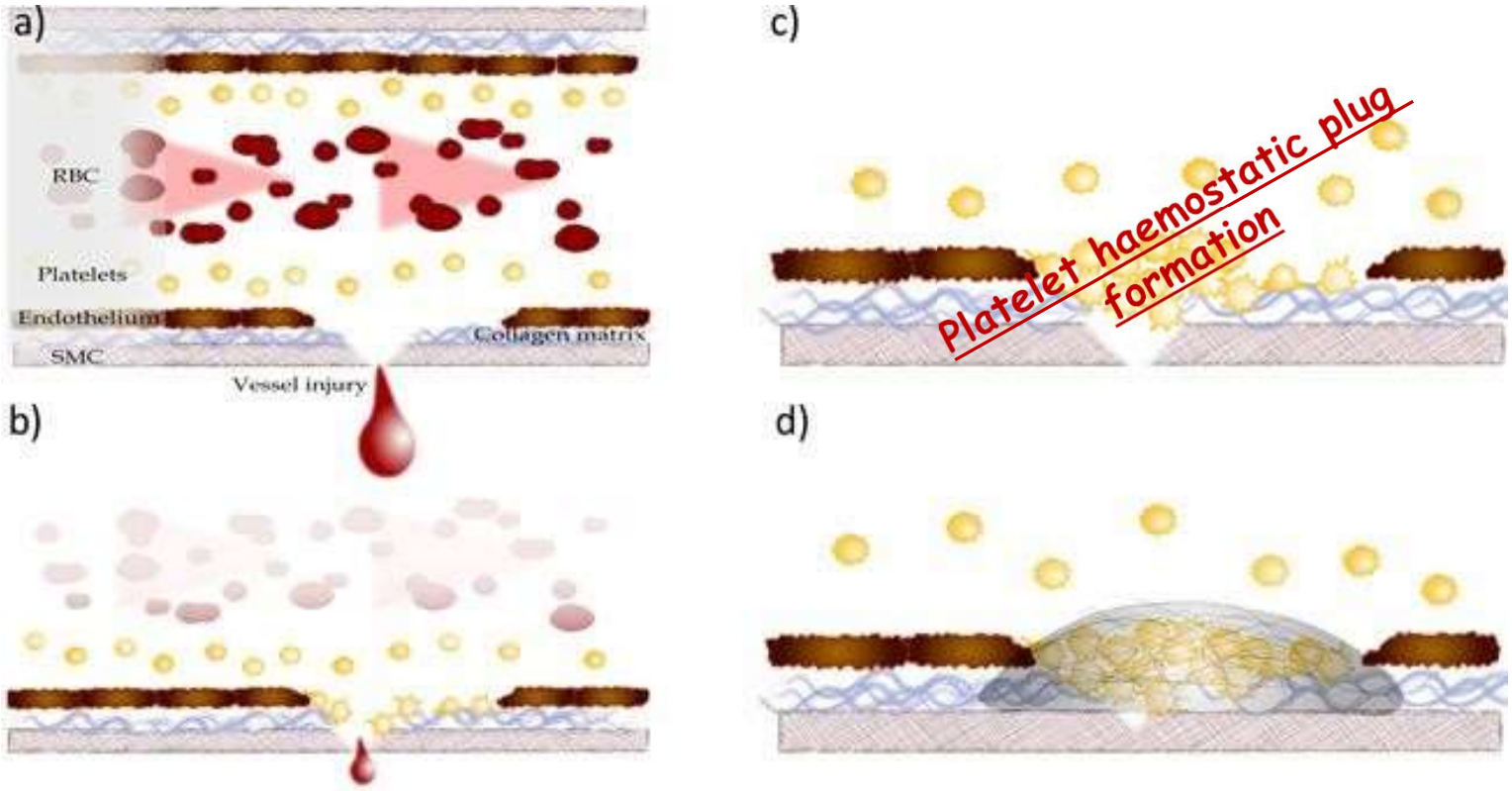
Steps of formation in bone marrow

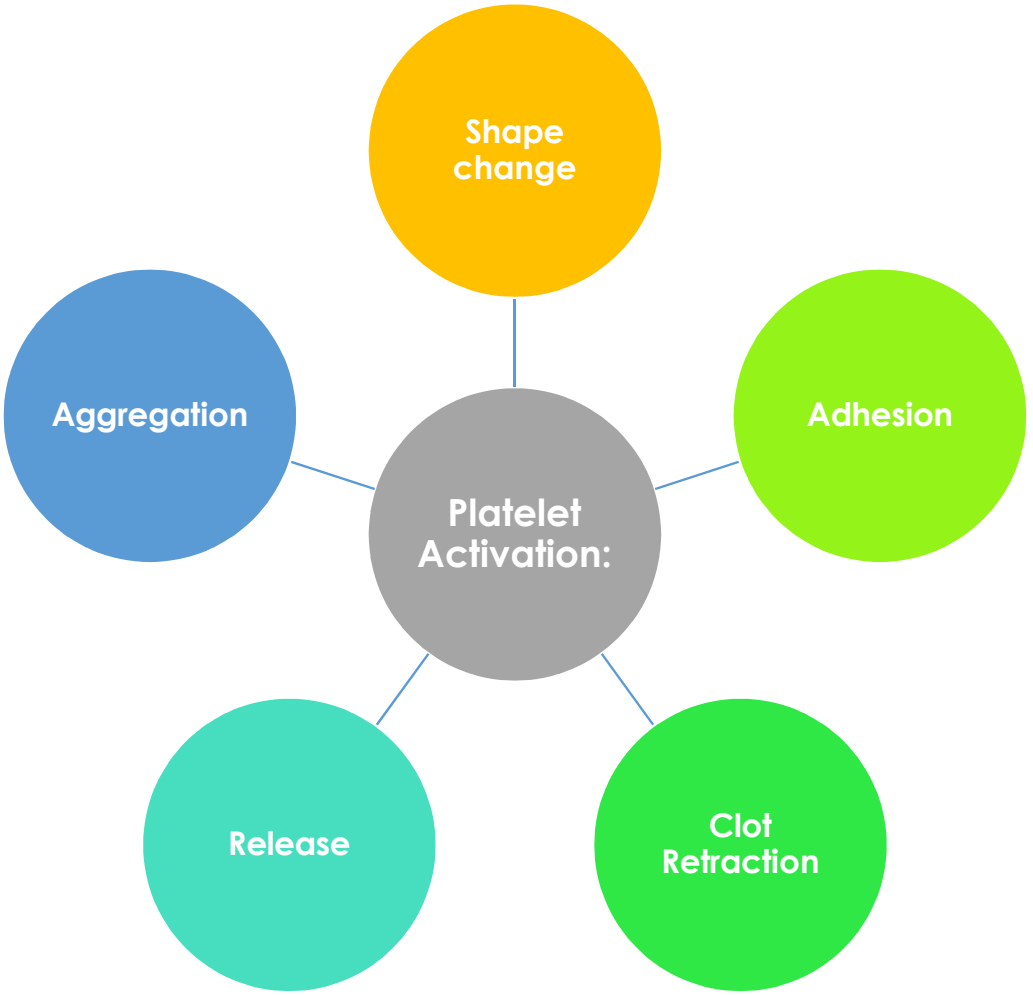


Platelet haemostatic plug formation



3-objective: Describe the role of platelets in hemostasis

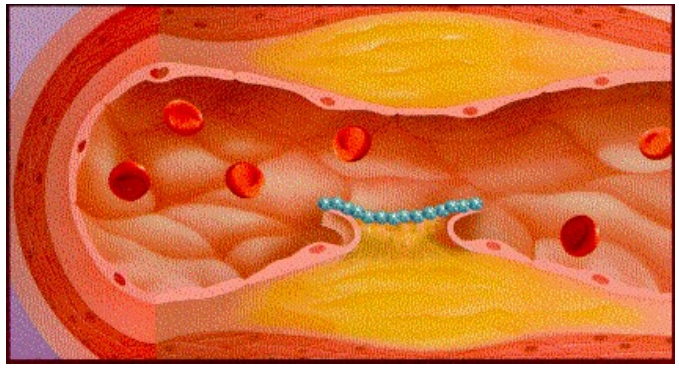
Platelet Functions begins with platelet activation



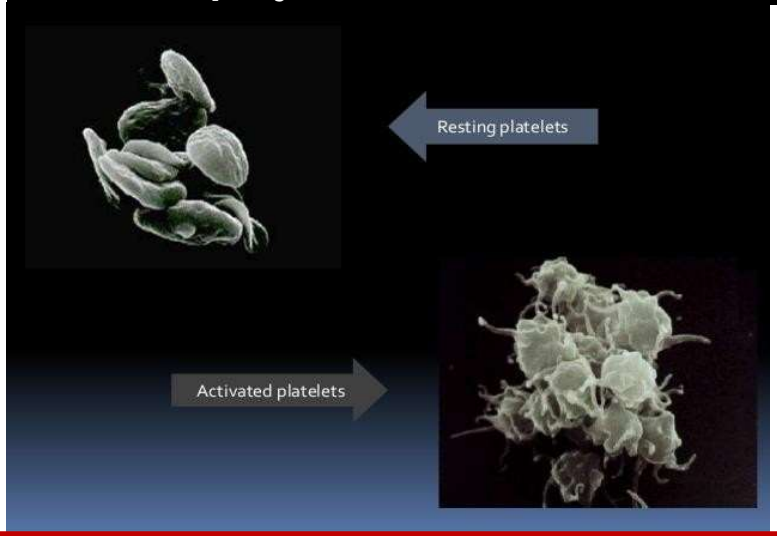
1-Platelet Adhesion

Adhesion:

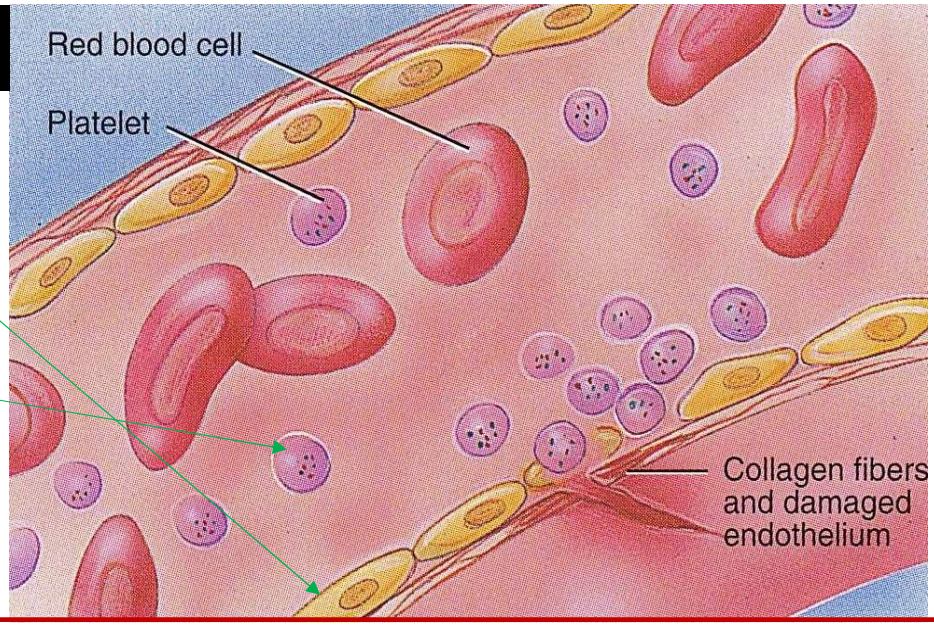
- Exposed collagen attracts platelets
- Platelets stick to exposed collagen underlying damaged endothelial cells in vessel wall



- **Platelets activated by adhesion**
- **Extend projections to make contact with each other**



جواها في كولاجين لو صار فيه انجري راح يطلع الكولاجين ولما يطلع راح يجذب الصفيحات لها، وعادة يكون بين الصفيحات تنافر على عكس لما يكون فيه انجري

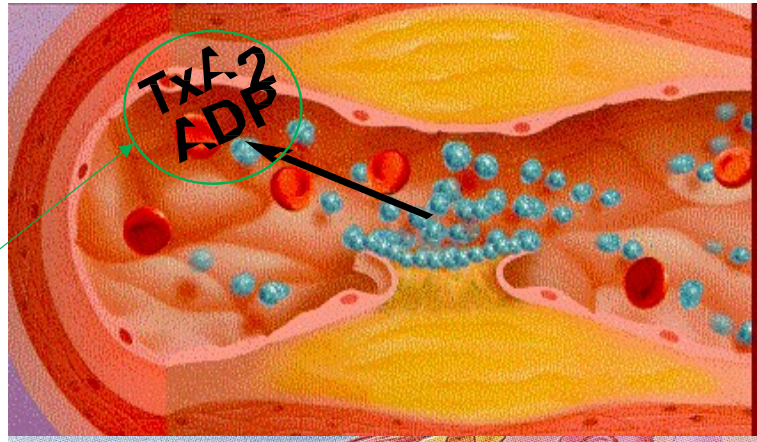


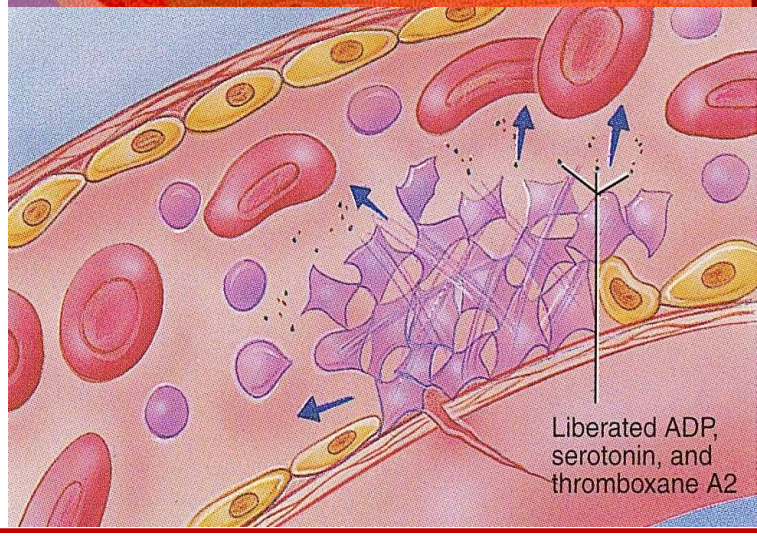
2-Platelet Release Reaction

•Activated platelets release Serotonin, ADP & Thromboxane A2

- **Serotonin & thromboxane A2 are vasoconstrictors decreasing blood flow through the injured vessel.**

راح ينشطون الصفيحات وبالتالي راح يتغير شكلها وبتصير more sticky وترتبط مع another platelet





Thromboxane A2 & ADP → Activate More platelets (**the stickiness**) → Adhere to original platelets → Platelet Plug

3-Platelet Aggregation

Thromboxane A2 & ADP → Activate More platelets (**the stickiness**) → Adhere to original platelets → Platelet Plug → Reinforced By Fibrin threads

Platelet Secretion:

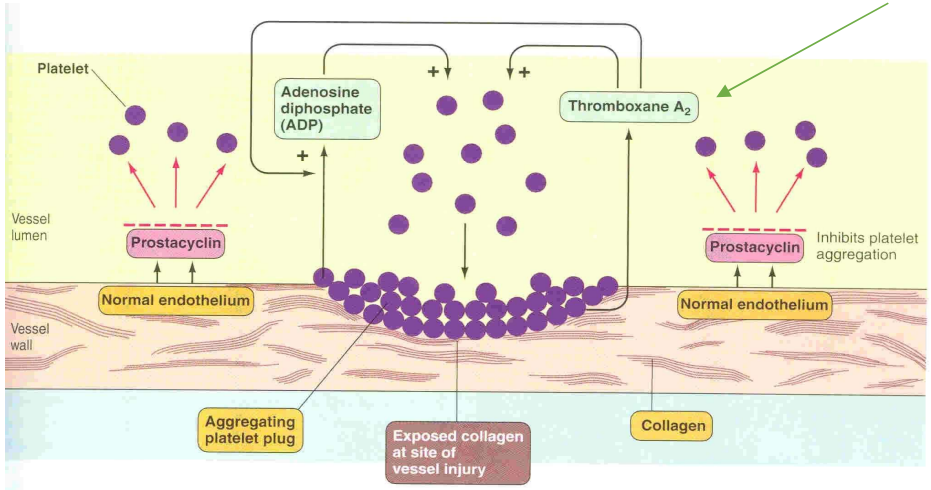
5HT	• Vasoconstriction
ADP	• Platelet Activation
Platelet Phospholipid	• Clot formation
Thromboxane A2	• Prostaglandin (Inhibited by Aspirin) • Vasoconstriction & platelet agggregation

(**TXA2**) is a prostaglandin formed from arachidonic acid

Why do platelets not attach to healthy Endothelium?

- Endothelium release prostacyclin and NO which Inhibit Aggregation

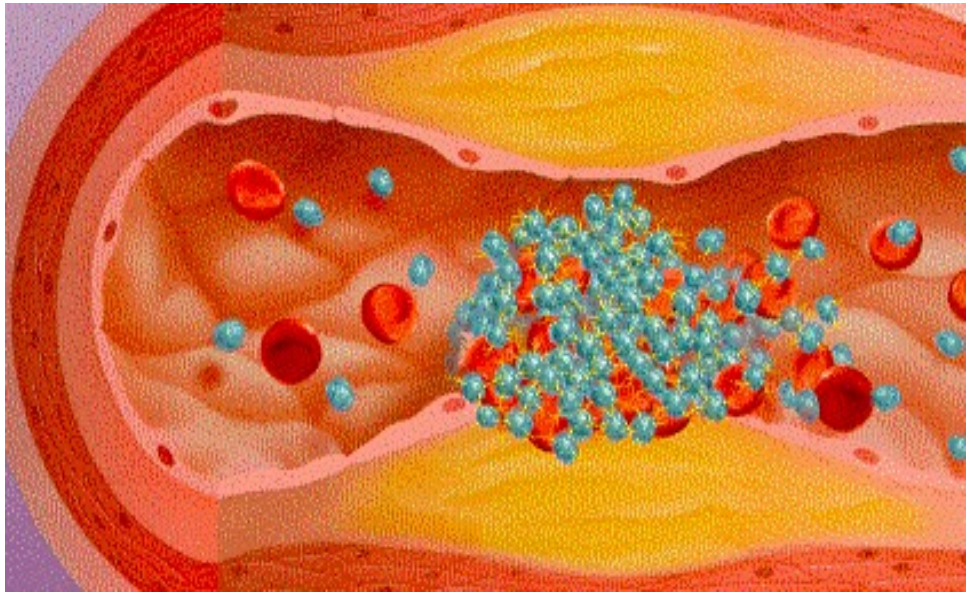
You can find more explanations in our twitter page



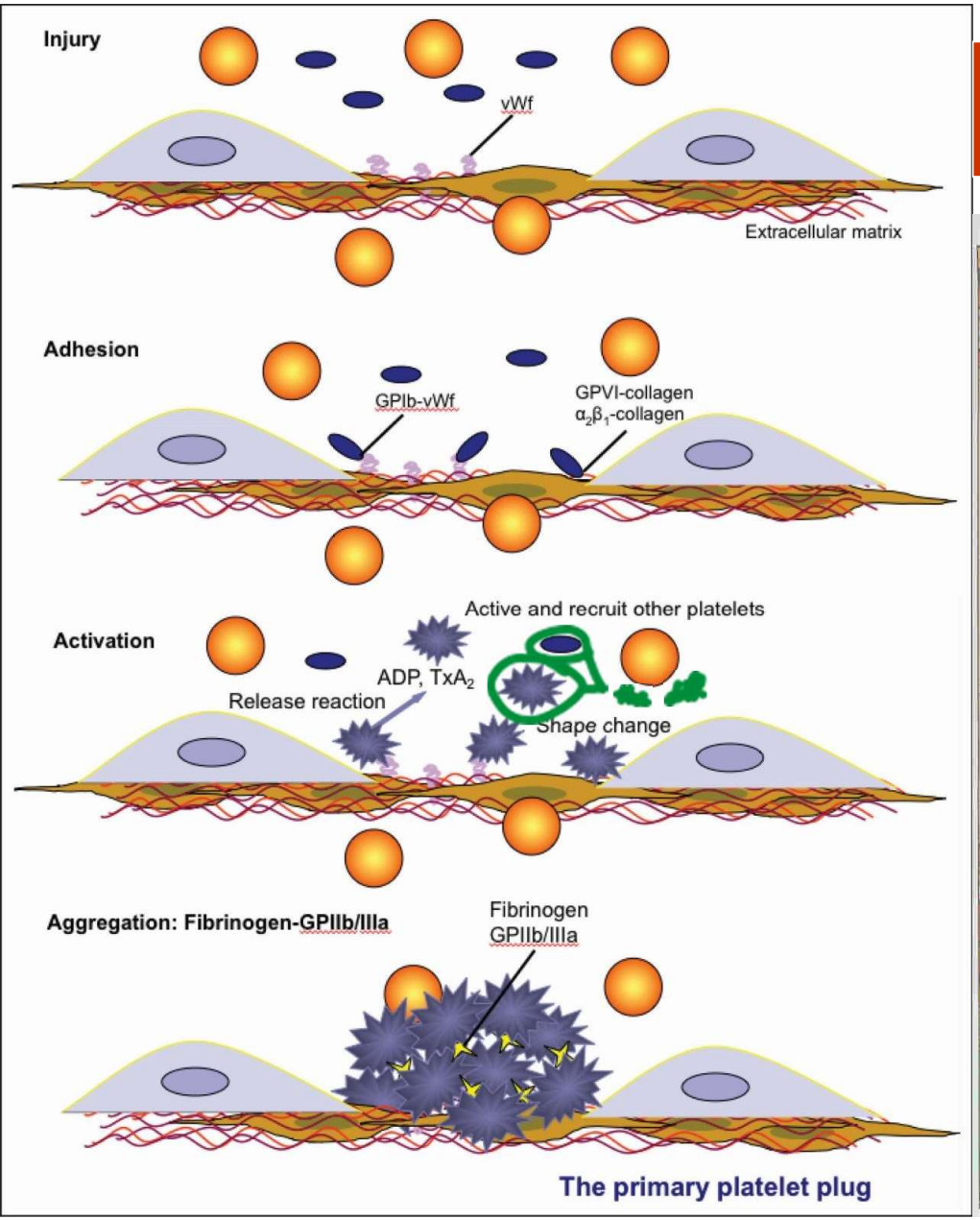
Platelet shape change and Aggregation

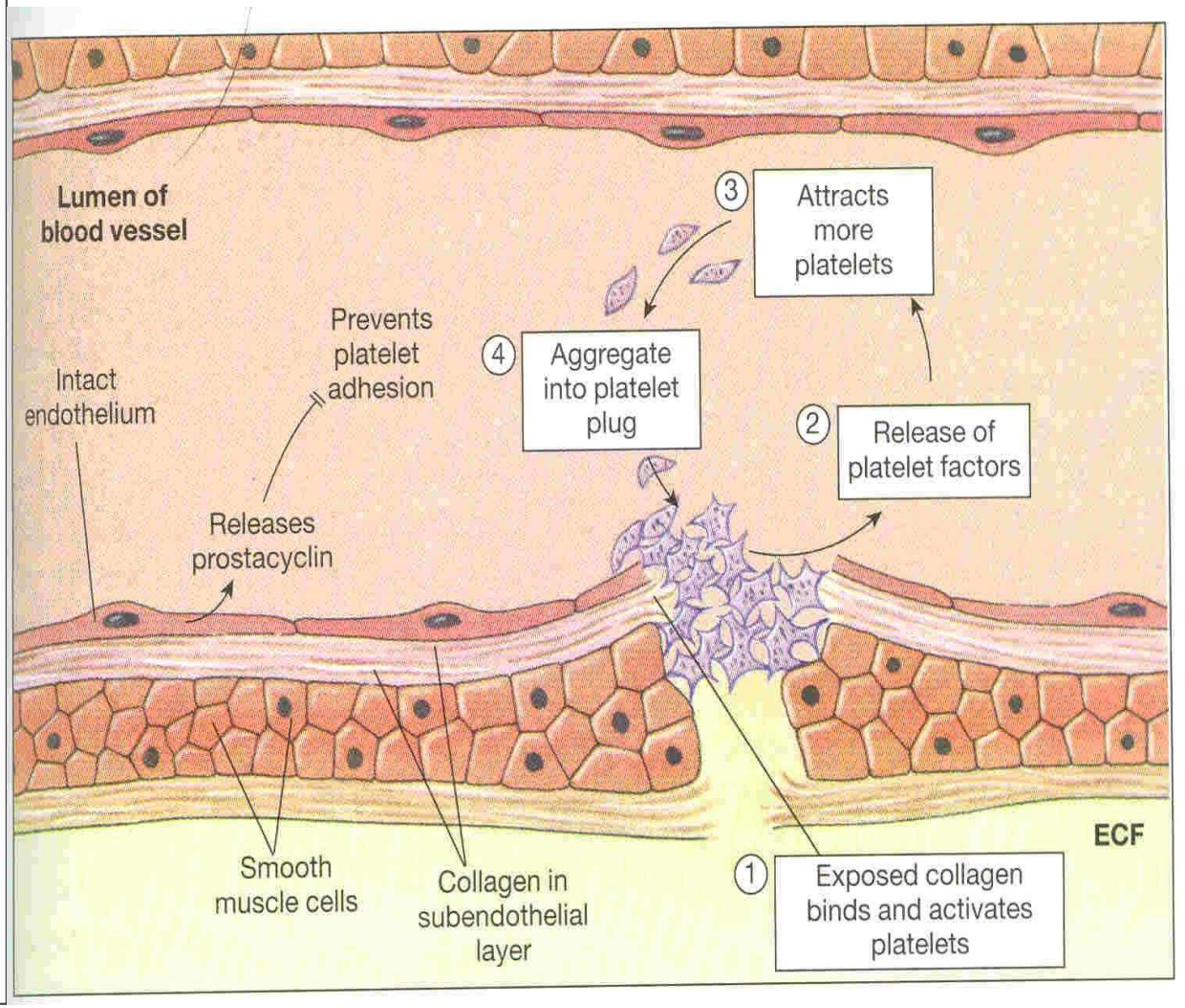
4. Platelet Activation

- **Clot Retraction:**
- Myosin and actin filaments in platelets are stimulated to contract during aggregation further reinforcing the plug and help release of granule contents.
- (Makes them sticky)

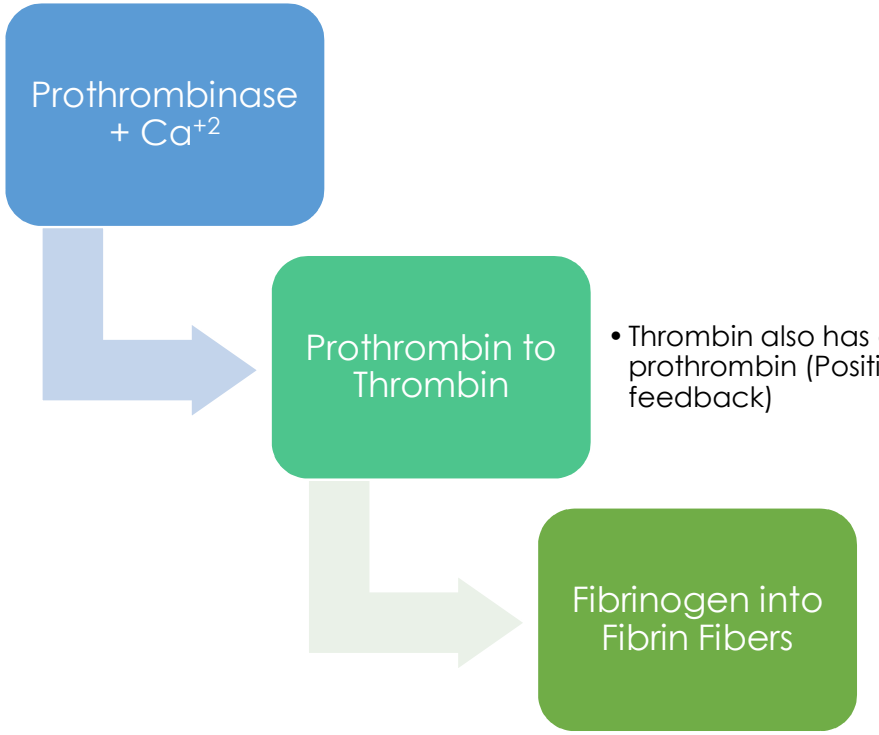


Platelet plug formation





Blood Coagulation (Overview)



- Thrombin also has an effect on prothrombin (Positive feedback)

2 Pathways form Prothrombin activator:

1. Extrinsic
2. intrinsic

Clotting Factors:

Table 37-1 Clotting Factors in Blood and Their Synonyms

Only factors you need to know

Clotting Factor	Synonyms
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; HMWK (high-molecular-weight kininogen)
Platelets	

You can find more explanations in our twitter page

Extrinsic:

Trauma to tissue

Release tissue thromboplastin
(Phospholipid + Lipoprotein)

Lipoprotein + Factor VII + Ca
activate Factor X (becomes Xa)

Factor Xa + Factor V + phospholipids
Form Prothrombinase

Prothrombin → Thrombin
- Thrombin activates Factor V (Positive feedback)

Intrinsic:

Initiation:
- Trauma to blood or exposure to collagen

Factor XII & Platelet Phospholipid
- Factor XII activated → XIIa
- Phospholipid contain platelet factor 3

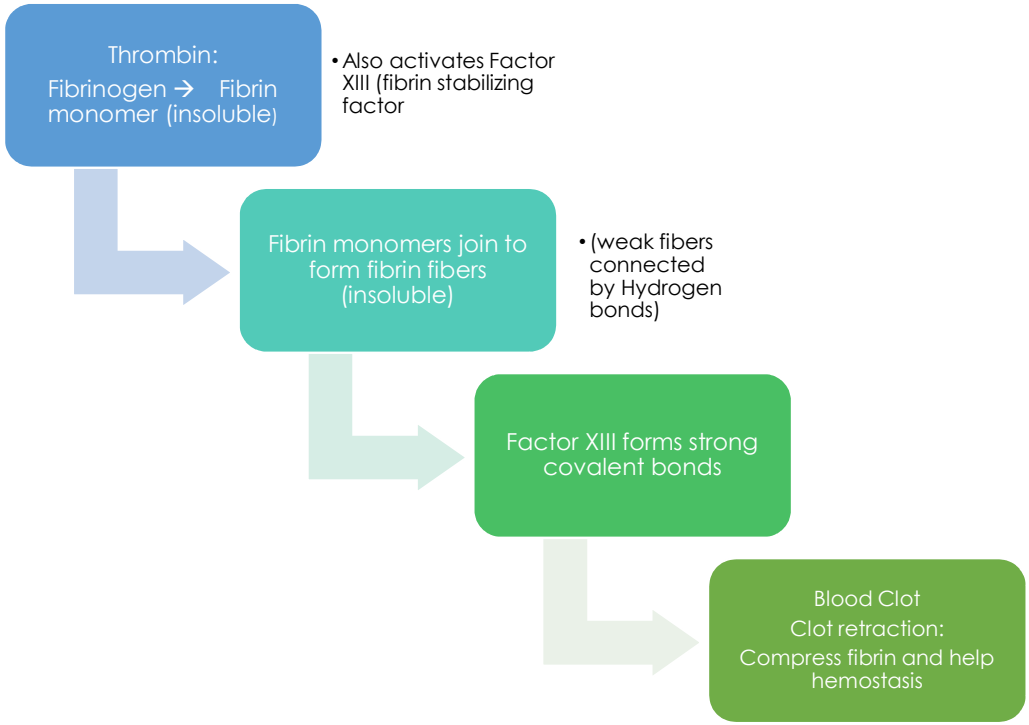
Activation of Factor XI
- Factor XII activates Factor XI → XIa
- Requires Kininogen + prekallikrein

Activation of Factor IX by XIa

Activation of Factor X
- Factor XIa + VIII + Ca+ activate Factor X

Factor Xa + Factor V + Phospholipids
- Prothombinase
- Same as Extrinsic

Final Common Pathway



Importance of Calcium:

- Used in every step except the first 2 steps of the intrinsic pathway.
- Causes acceleration.

Role of Vitamin K:

- Clotting requires vitamin K
- Fat soluble
- More bile → more absorption of Vit K

Synthesis of 4 factors:

1. Factor X (10)
2. Factor IX (9)
3. Factor VII (7)
4. Factor II (prothrombin) (2)

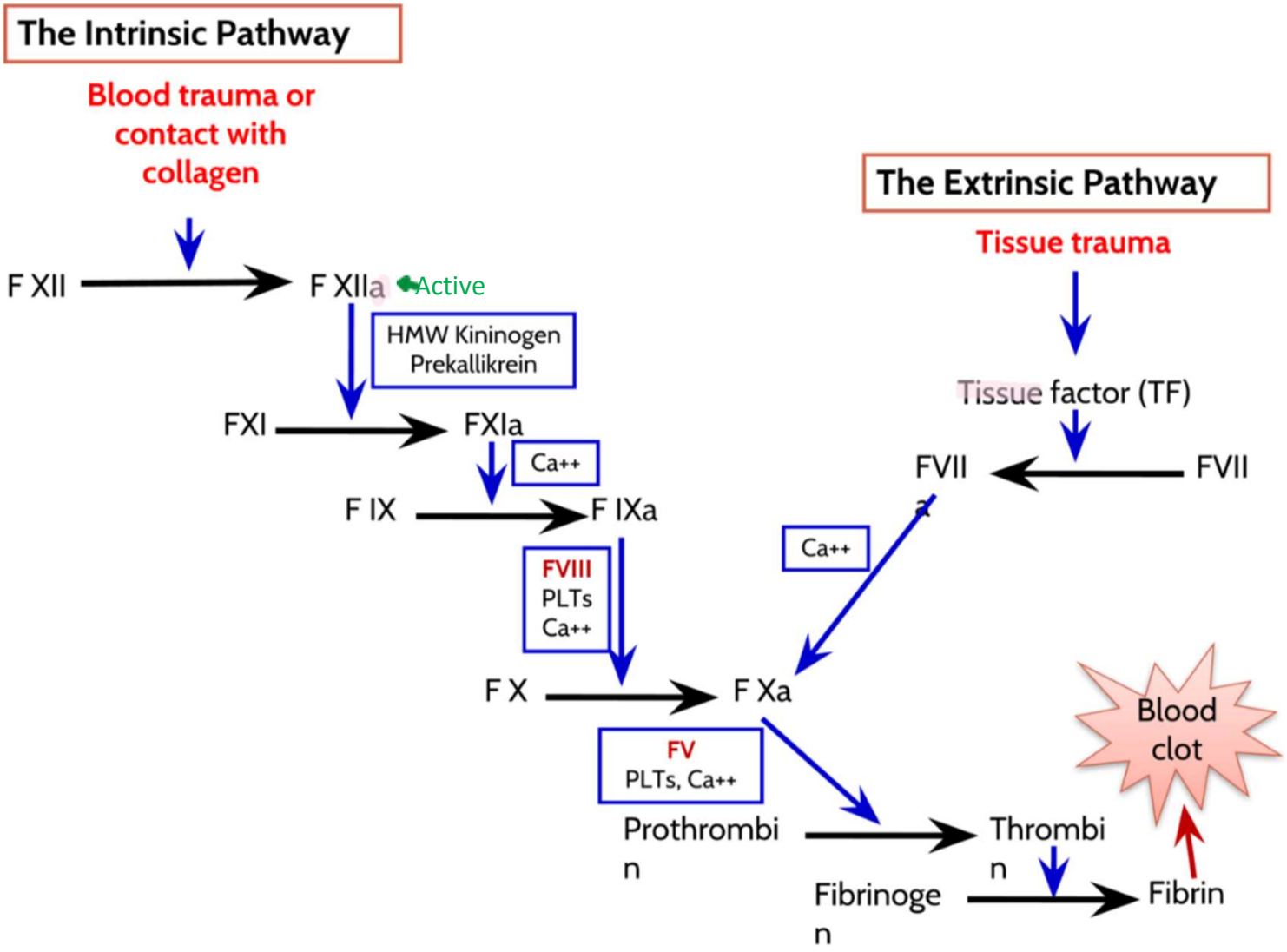
To remember: (1972)

Produced by GIT normal flora

How to stop samples from clotting?

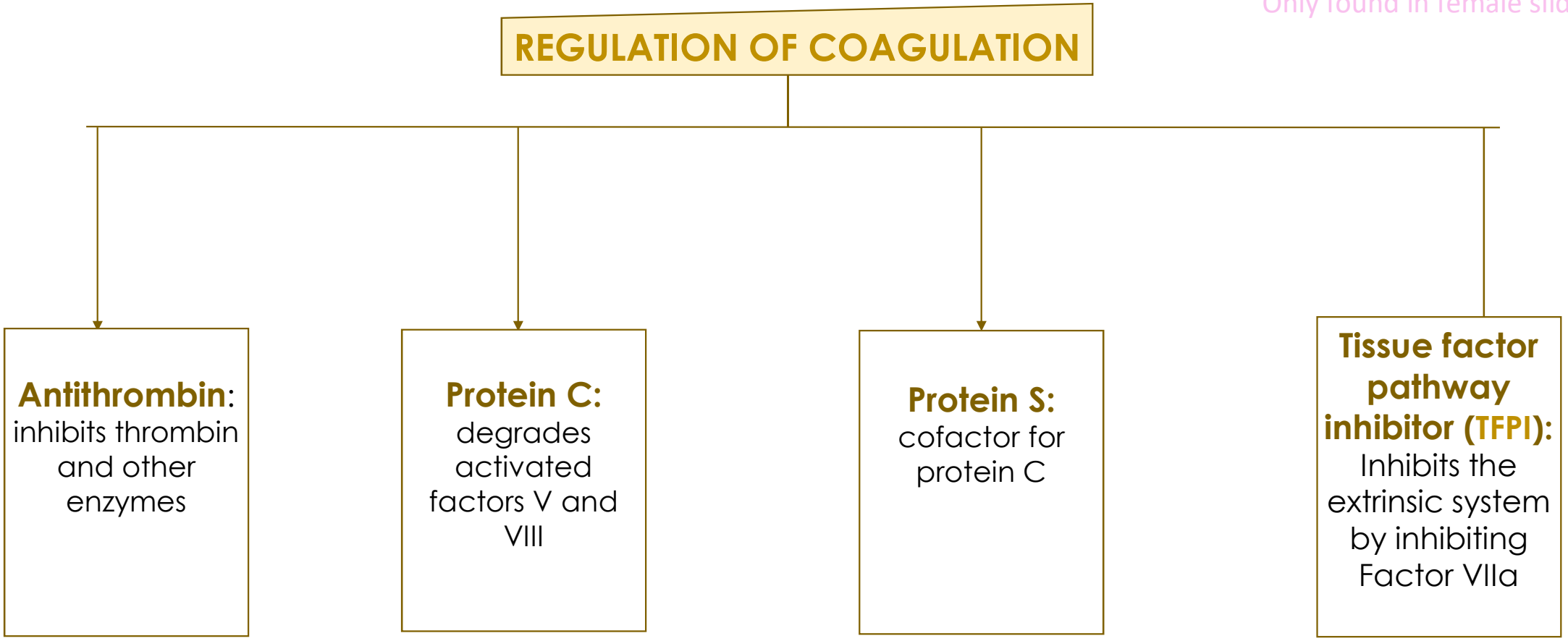
1. Citrate Ions → Deionize Calcium
2. Oxalate Ions → Precipitate Calcium

- No Calcium → No Clotting


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

Only found in female slides

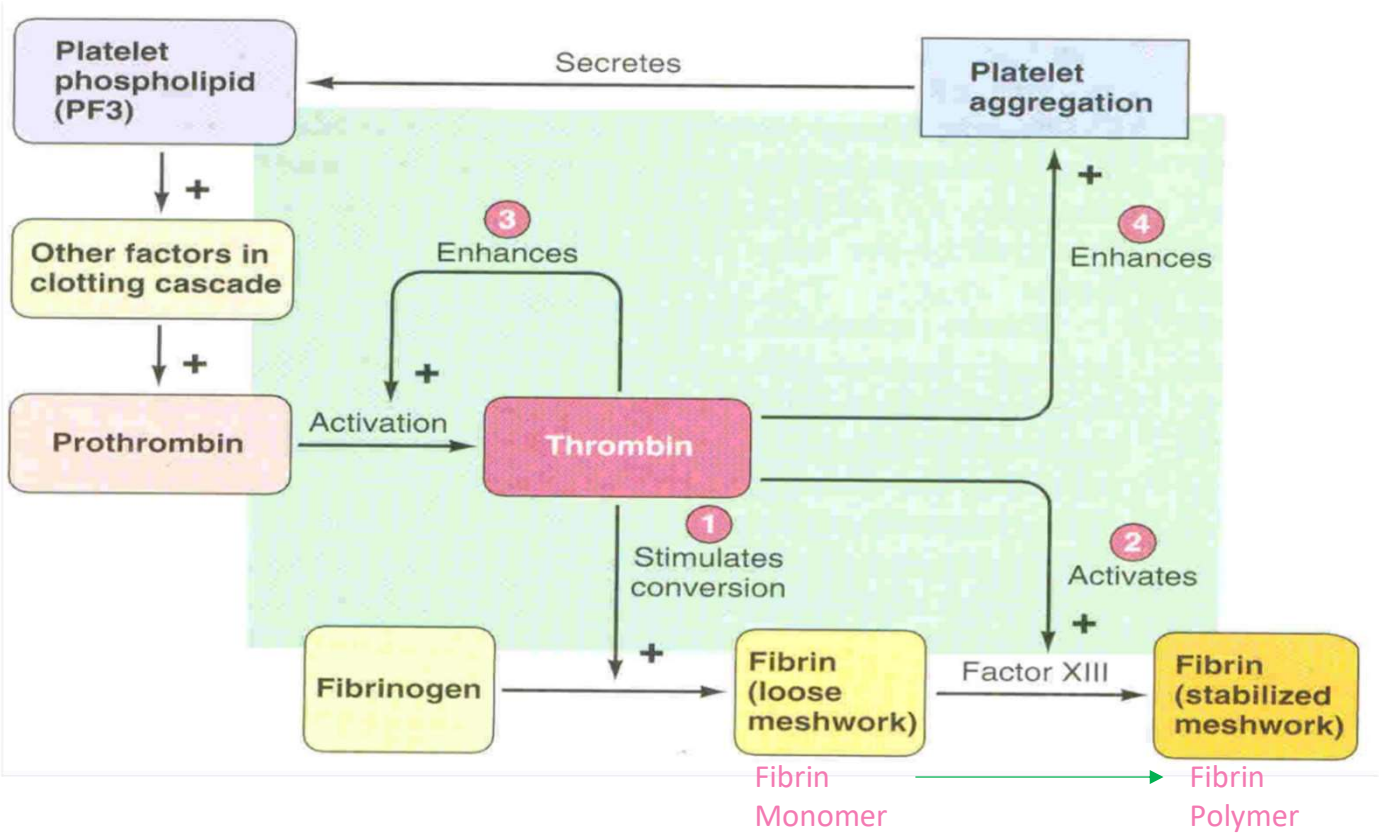
REGULATION OF COAGULATION



Deficiency of any of these proteins can increase risk of thrombosis

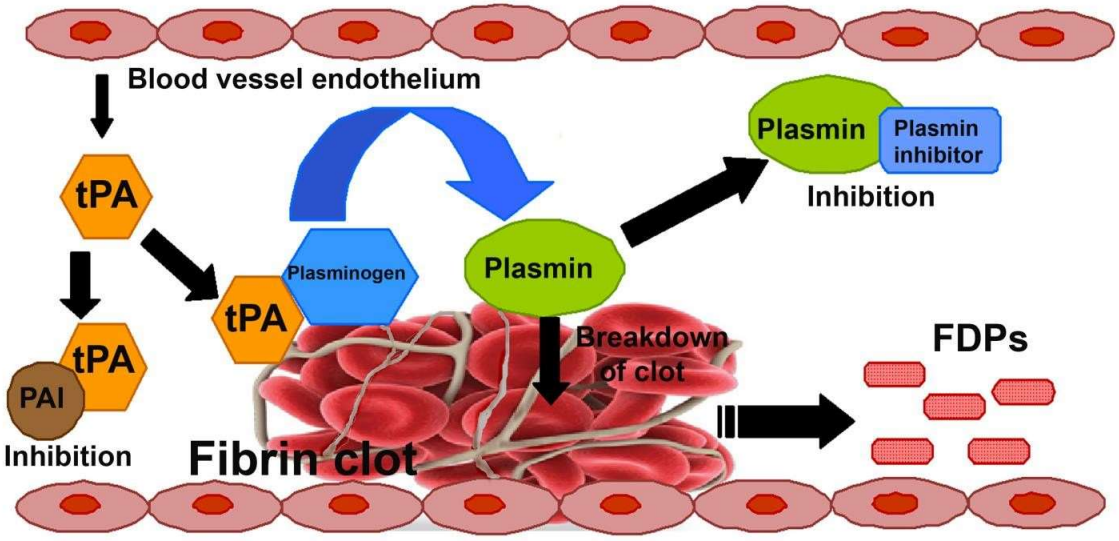
Roles of Thrombin (+ve feedback)

- Fibrinogen to Fibrin
- Activate Factor XIII and V
- Thrombin is essential in platelets morphological changes to form primary plug
- Thrombin stimulates platelets to release ADP &thromboxane A2; both stimulates further platelets aggregations



Fibrinolysis

1. Clot forms
2. Plasminogen is trapped in clot
3. Endothelium releases tissue plasminogen activator (t-PA)
4. Plasminogen → Plasmin
5. Dissolve clot and coagulants (Factor V, VII, II, and XII)
6. Fibrin break down into Fribrin degradation products (FDP)



Plasmin is controlled by Plasminogen Activator Inhibitor (PAI)

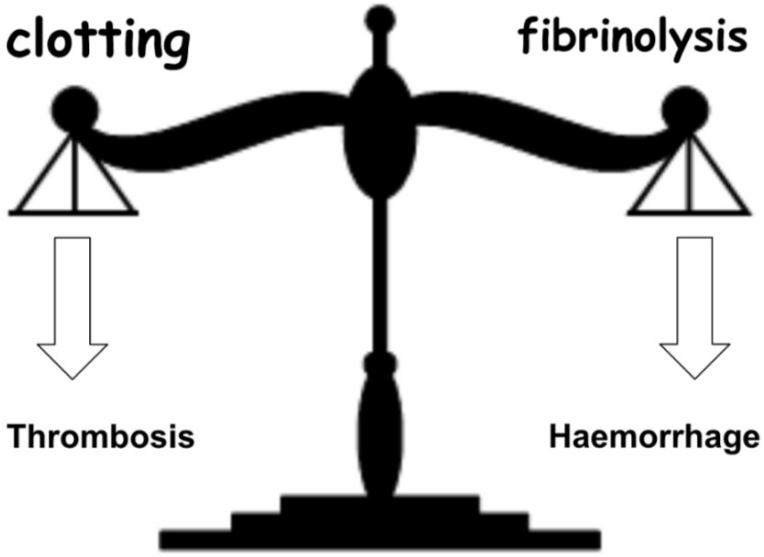
Clotting VS Fibrinolysis

- Procoagulant – Promote Coagulation (Fibrin Stabilizing Factor XIII)
- Anticoagulant – Inhibit Coagulation (Heparin)

Normally, there is more anticoagulant in the blood stream. Once an injury occurs, procoagulants are activated and override anticoagulants.

Anticoagulants:
Heparin: Prevent conversion
Prothrombin → Thrombin

Warfarin:
Prevent Synthesis of Factors: II, IX, X, VII



Bleeding disorders:

More explanation in next slides

Platelet defects:

- Thrombocytopenia
- Low number of platelets
- Small Hemorrhages all over the body
- No clot retraction

Coagulation factors defect:

- Hemophilia
- More bleeding
- X-linked disease (Affects males)
- Hemophilia A: Factor VIII deficiency
  Hemophilia B: Factor IX deficiency

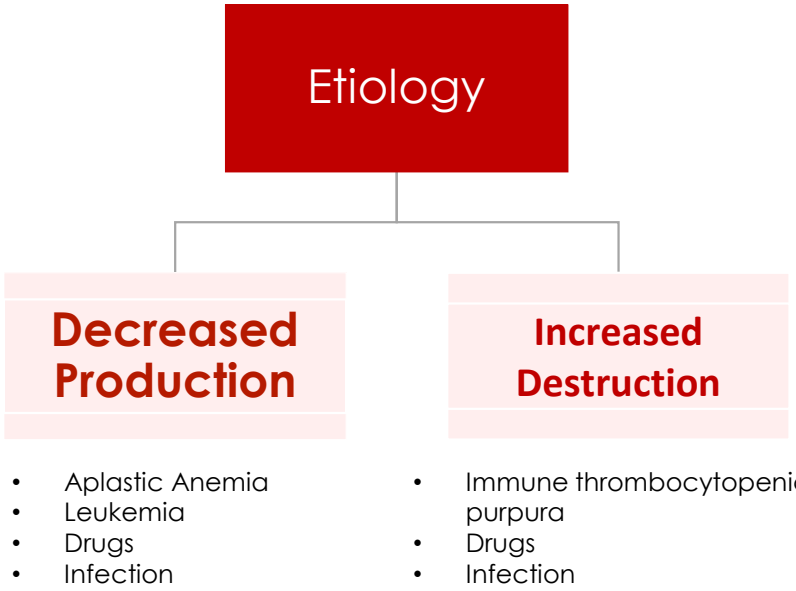
Vitamin K deficiency/ Liver disease:

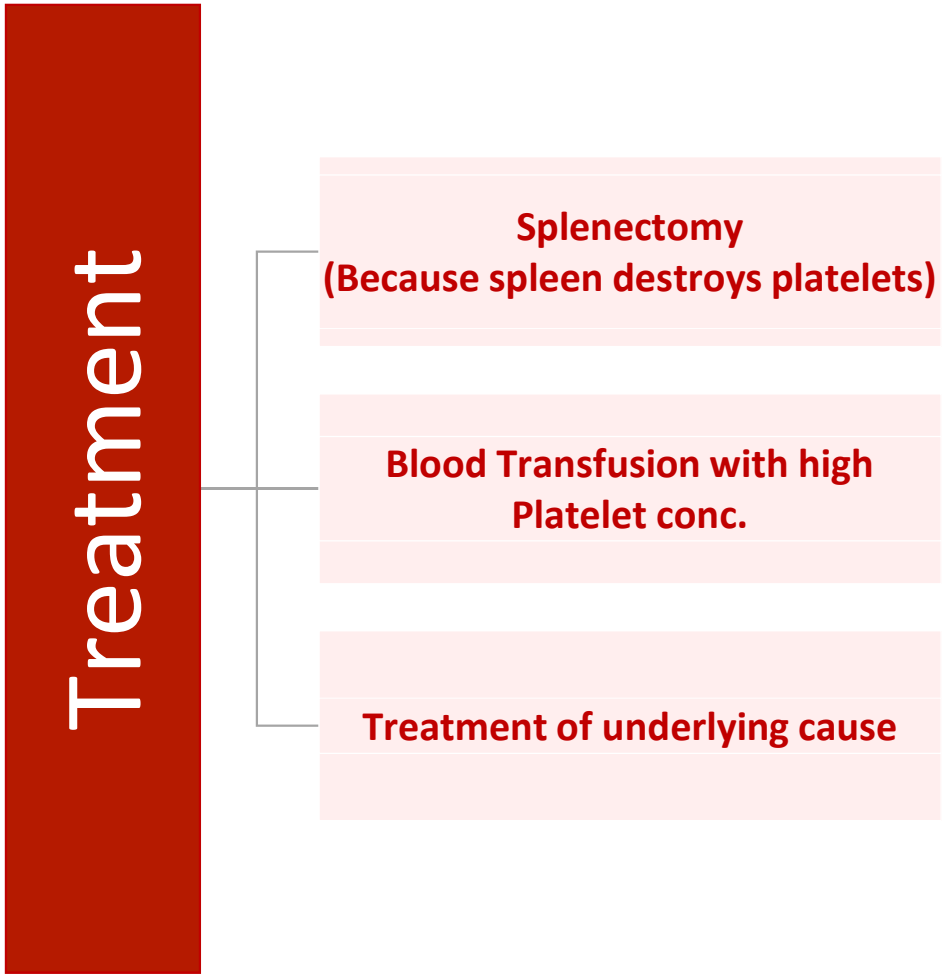
- All coagulation factors are synthesized in the liver
- Vitamin K is essential for synthesis
- Factors X, IX, VII, and II
- Vitamin K produced by GIT bacteria

Only found in male slides

Thrombocytopenia

- Platelet count drops to 50,000/µL
- Normal: 150,000 – 400,000 /µL
- Fatal: Below 10,000 /µL





Hemophilia (Bleeding disease)

- Hemophilia A:

1. 85% of cases
2. Deficiency of factor VIII

- Hemophilia B:

1. 15% of cases
2. Deficiency of factor IX

- Clinical features:

1. Bruising
2. Massive bleeding
3. Hemorrhage in joints

Caused by genetic disorder in the X chromosomes. Affects males.

Treatment:
Injection:
Hemophilia A → Factor VIII
Hemophilia B → Factor IX

Liver diseases & Vitamin K deficiency

- Liver:
- Hepatitis – Liver inflammation
- Cirrhosis – Loss of liver cells

1. Most factors are produced in Liver
2. Decrease clotting factors
3. Increase clotting time

- Vitamin K: Required for the synthesis of:

1. Factor II – Prothrombin
2. Factor VII
3. Factor IX
4. Factor X

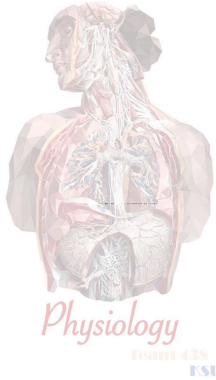
Remember 1972

Quiz

Q1-Which of the following is the correct sequence of events leading to blood clotting?			
A) vasoconstriction, platelet aggregation, coagulation	B) platelet aggregation, vasoconstriction, coagulation	C) vasoconstriction coagulation platelet aggregation	————
Q2-Which of the following is involved in the final phase of blood clotting?			
A) formation of fibrin	B) formation of prothrombin	C) activation of blood clotting factor X	—————
Q3-Converts fibrinogen to fibrin			
A) Plasmin	B) thrombin	C) 5HT	D) ADP
Q4-The Vitamin K dependent factors are:			
A) II, XII, IX, XIII	B) VII, V, IX, X	C) I, VI, IX, X	D) II, VII, IX, X
Q5-Clots form to stop the "leakage" of blood from a damaged vessel. After the damaged vessel has healed, the clot is no longer needed and goes through a process of dissolution. Which of the following is involved in the dissolution of a clot?			
A) plasmin	B) fibrinogen	C) thrombin	—————

Key answers:

1. A
2. A
3. B
4. D
5. A



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• زياد الدوسري	• ديما المزيد
• محمد الحمد	• جود الخليفة
• فيصل القفاري	• جود العتيبي
• عبدالله باسمح	• رغد المبارك
• جهاد العريني	• ريناد المطوع
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	• مي بابعير
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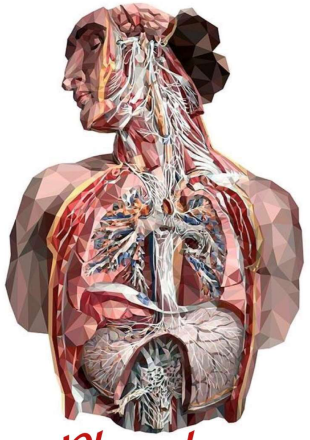

Team leaders:

- عمر الشيناوي
- ايلاف المسيحل