PHYSIOLOGY TEAM 435

12 Hemostasis

- Very important
- Extra information
- Terms

هذه المحاضرة تستحق التأمل في إعجاز خلق الله حيث أن الصفائح الدموية وهي آخر خلية اكتشفها العلماء مسؤولة بشكل كامل عن تضميد الجروح وبدونها نحن معرضون للنزيف حتى الوفاة من أبسط جرح فسبحان الله !

الملاحظات المشروحة وضعت لتثبيت المفاهيم وللتوضيح لكن أغلبها مهم لذلك يفضل الاطلاع عليها.

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Objectives

1. Describe formation and development of platelet.
2. Recognize different stages of hemostasis.
3. Describe the role of platelets in hemostasis.
4. Recognize different clotting factors.
5. Describe the cascade of clotting .
6. Describe the cascade of intrinsic pathway.
7. Describe the cascade of extrinsic and common pathways.
8. Recognize the role of thrombin in coagulation.
9. Recognize process of fibrinolysis and function of plasmin

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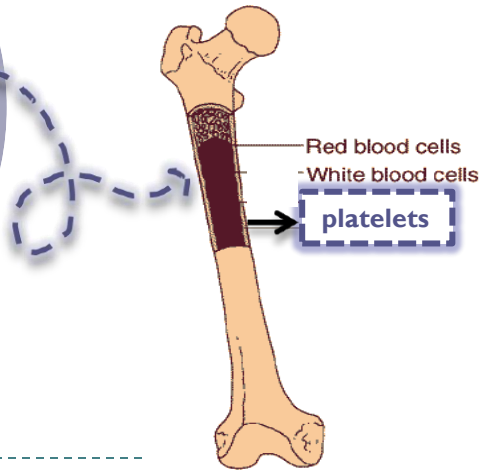
Platelets formation

Thrombocytes (Platelets): fragments of megakaryocytes

Remember: RBCs are formed when stem cell is developed to a RBC

But megakaryocytes DOES NOT transform to platelets instead it will rupture "fragments" after entering the blood to very small pieces that are platelets

Site of formation: bone marrow



Regulation of Thrombopoiesis by : Thrombopoietin

Remember: Regulation of Erythropoiesis by Erythropoietin

(Erythropoietin is formed in kidney & liver , while Thrombopoietin in liver)

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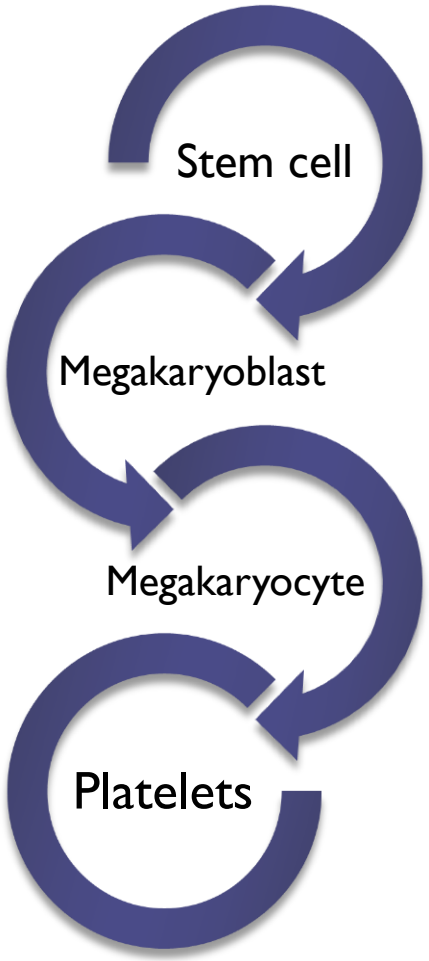
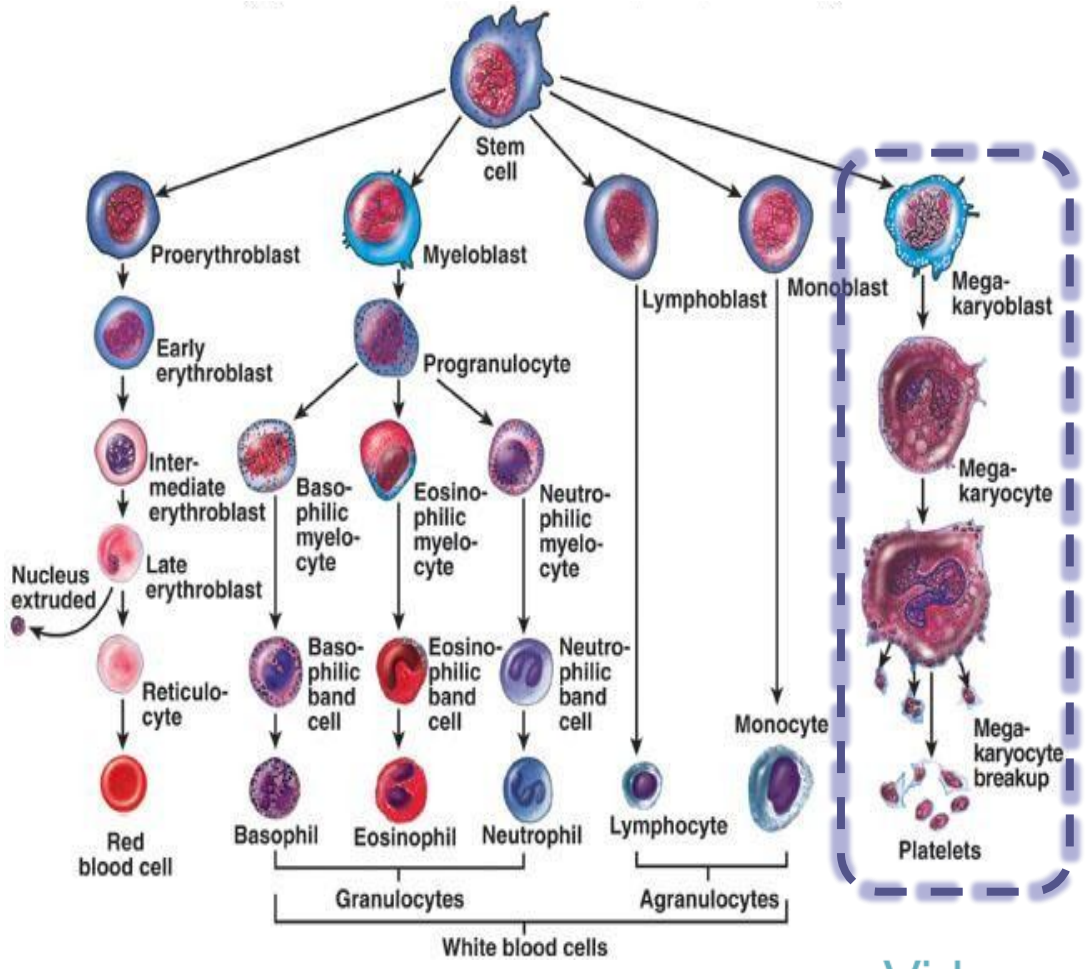
Steps of Platelets formation

Megakaryocyte is an extremely large cells





Every Megakaryocyte gives rise to 1000 platelets

Video

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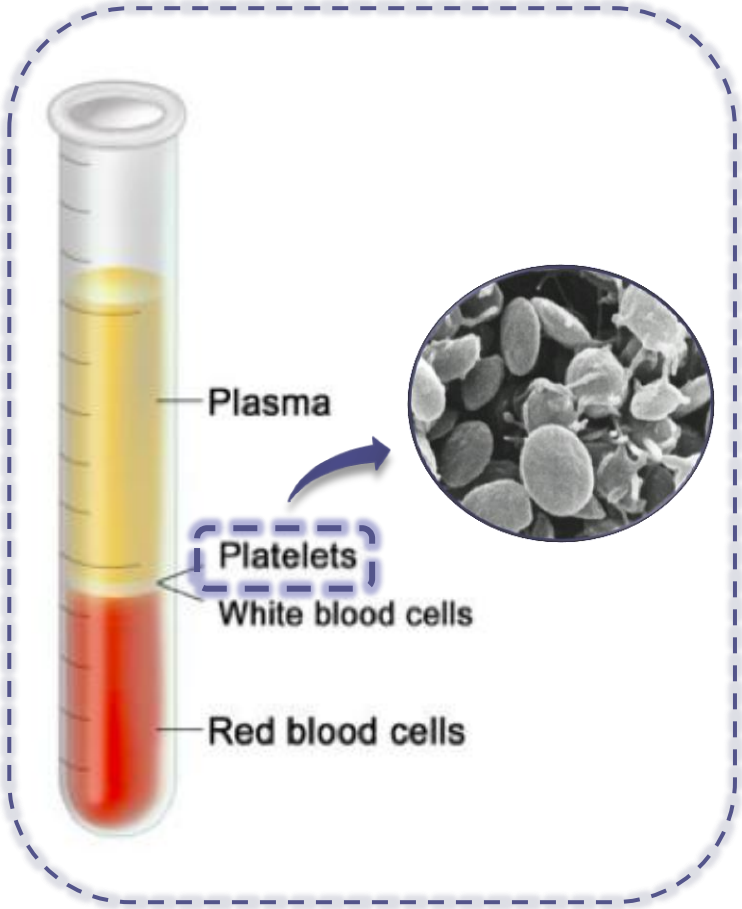
Thrombocytes



Platelets count:
150,000 – 450,000
(RBCs > Platelets > WBCs)

Life span of platelets =
8-12 days

Exist in the buffy coat with percentage =
1%

Platelets

Platelets are less than RBCs because we need red blood cells all the time (they provide oxygen) but we need platelets only at the time of injury

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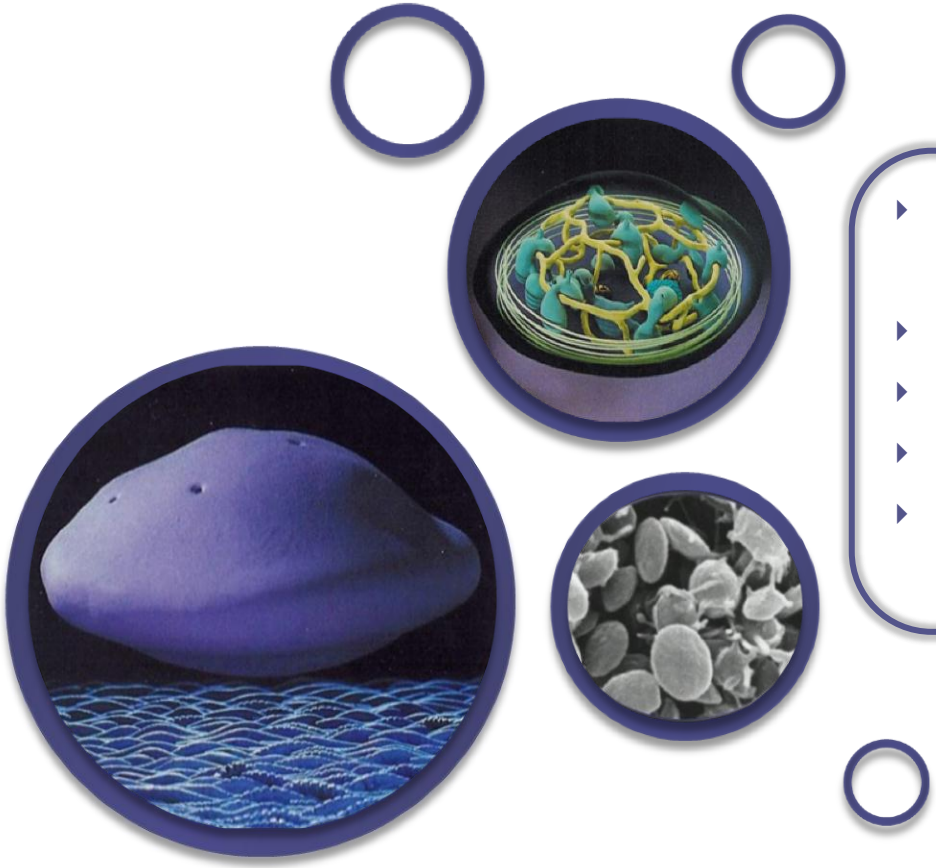
Platelets structure



- Platelets (Thrombocytes) have biconcave disc.
- Have smooth surface "Endothelial"
- They are 1- 4 micrometers in diameter.
- They do not have nucleus
- They have mitochondria and other cellular components.

- They are also contain : (Actin and Myosin proteins) similar to those found in muscle cells
- These proteins are very important for contraction
- platelets are known as " small muscle cells" because they contract exactly like muscles.

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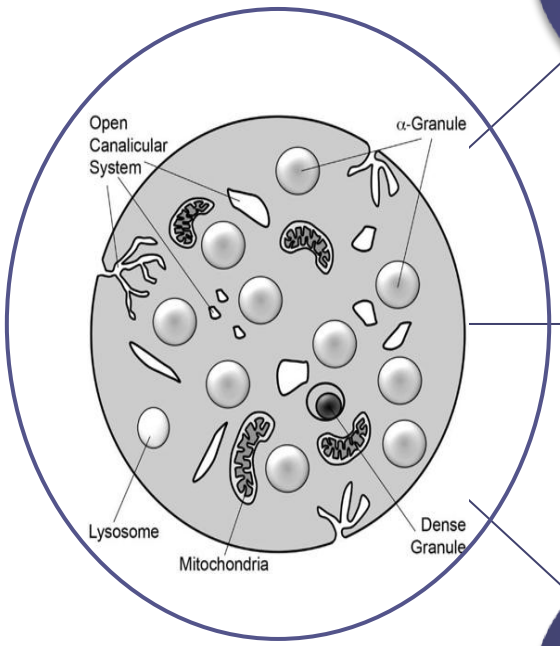
Platelets contents

Active cells (alpha granule)

Contain :
1. contractile proteins
2. Fibrinogen
3. Von Willebrand factor (vWF)
4. other proteins



Dense granules

Contain :
1. High calcium content
2. Rich in ADP
3. Serotonin

(نعتبرها أكياس تحملها الصفائح الدموية وتستخدمها وقت الحاجة)

open canals system

They are pores which dense granule comes out from it

(ذكرنا أن الصفائح الدموية لديها أكياس تستخدمها وقت الحاجة، هذه الأكياس من أين تخرج؟ من خلال هذه الثقوب).

platelets also contain Growth Factors that eventually helps repair damaged vascular walls .

vWF is a blood glycoprotein involved in hemostasis.

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Hemostasis

Hemostasis:

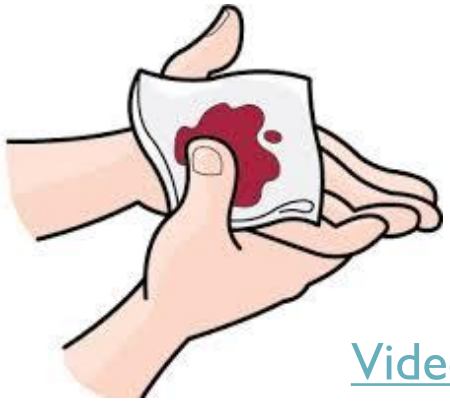
The spontaneous arrest of bleeding from ruptured blood vessels.

Hemo = Blood.
Stasis = Standing or stopping.

Hemostasis = to stop bleeding While :
Homeostasis = balance

Note : always remember when we talk about hemostasis we want to stop bleeding.

- There are daily trauma that effect blood vessels without any symptoms and we are not aware of them because of our hemostatic system, if it did not stop it will cause a huge damage such as brain hemorrhage.



Video

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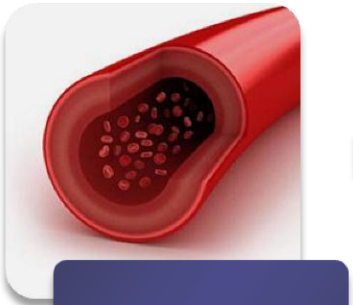
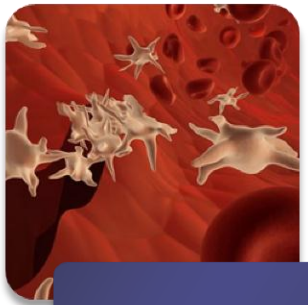
Mechanism


Vessel wall


Platelet


Blood coagulation


Fibrinolytic system

بداية لتكون لديكم نظرة شاملة عن المحاضرة قبل التوغل في تفاصيلها يرجى مشاهدة المقطع أدناه (أثناء رحلتنا في عملية تجلط الدم ورجوع المنطقة المصابة إلى حالتها قبل الجرح ، ضعوا في أذهانكم صورة الطفل الموجود بالمقطع والجرح الذي تعرض إليه لتتخيلوا جميع المراحل التي سيمر بها والتي ستنتهي بالتئامه تماماً).

Video

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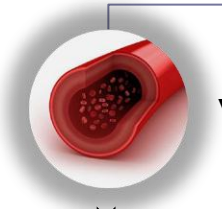
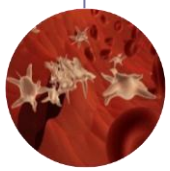
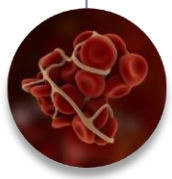
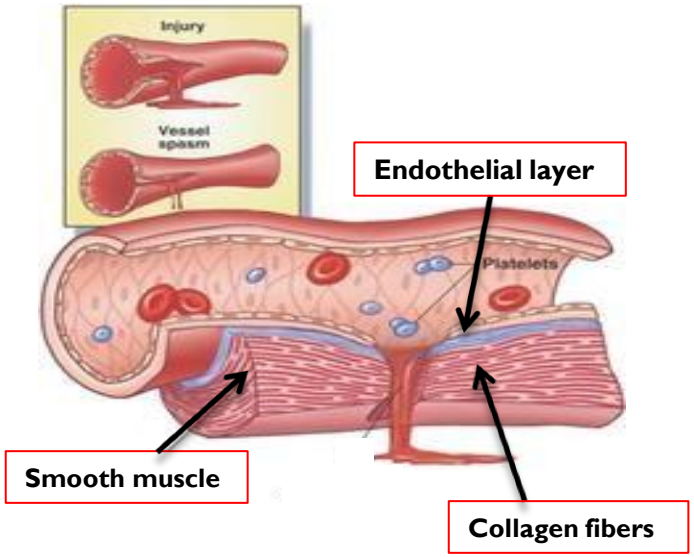
Hemostatic mechanisms


Vessel wall


platelets


blood coagulation


Fibinolytic system



هذه العملية عبارة عن انقباض في الوعاء الدموي للمساعدة في تخفيف النزيف

Immediately after injury a localized : **Vasoconstriction**

Components of blood vessel : Endothelial cells , collagen , smooth muscle.

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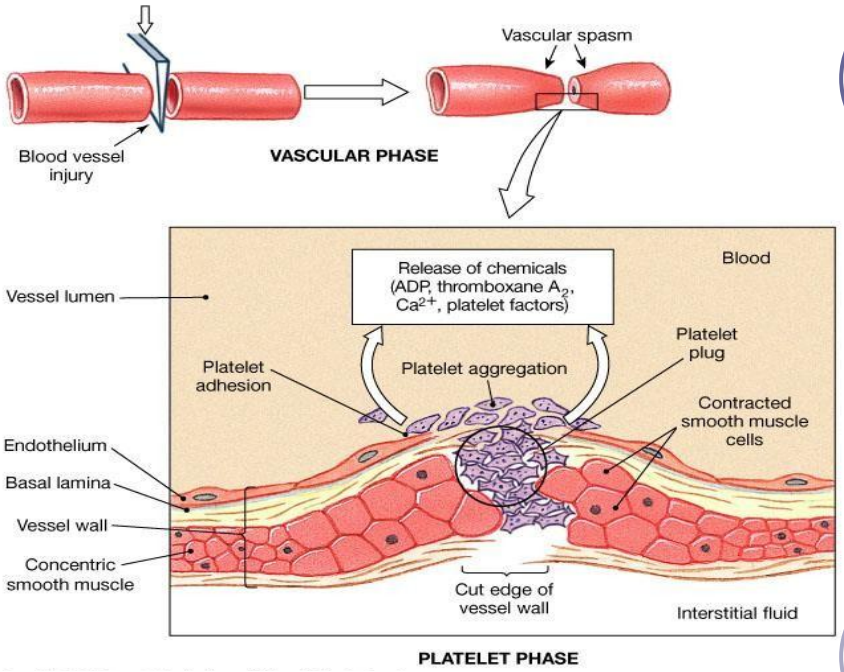
Vessel wall



Mechanism:

1. **Systemic release of adrenaline**
   "Hormonal ➡ Helps vessel contraction"
2. **Nervous Factors**
   "Stimulation for nerve impulses + nerve reflex is vasoconstriction"
3. **Local release of : thromboxane A2 & 5TH "Serotonin" ➡ By platelets**
   "For smaller vessels"
4. **Crushing injuries ➡ Intense spasm ➡ No lethal loss of blood**

Vasoconstriction
will not stop bleeding it only decrease it and helps the next step -platelet phase-

Video

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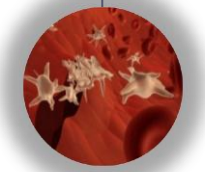
Hemostatic mechanisms

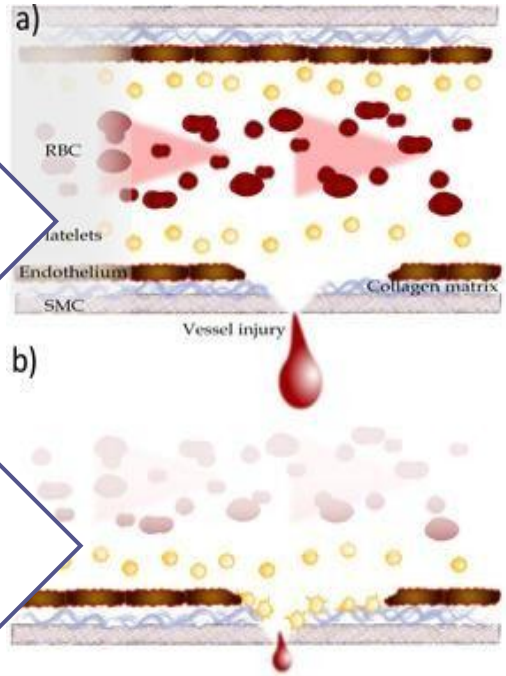

Vessel wall


platelets


blood coagulation


Fibinolytic system

Platelet haemostatic plug formation



Rupture

بعد ما تجمعت الـplatelets يقل النزيف

تتغير شكلها وبدت تتجمع بمكان الـinjury

Platelet plug

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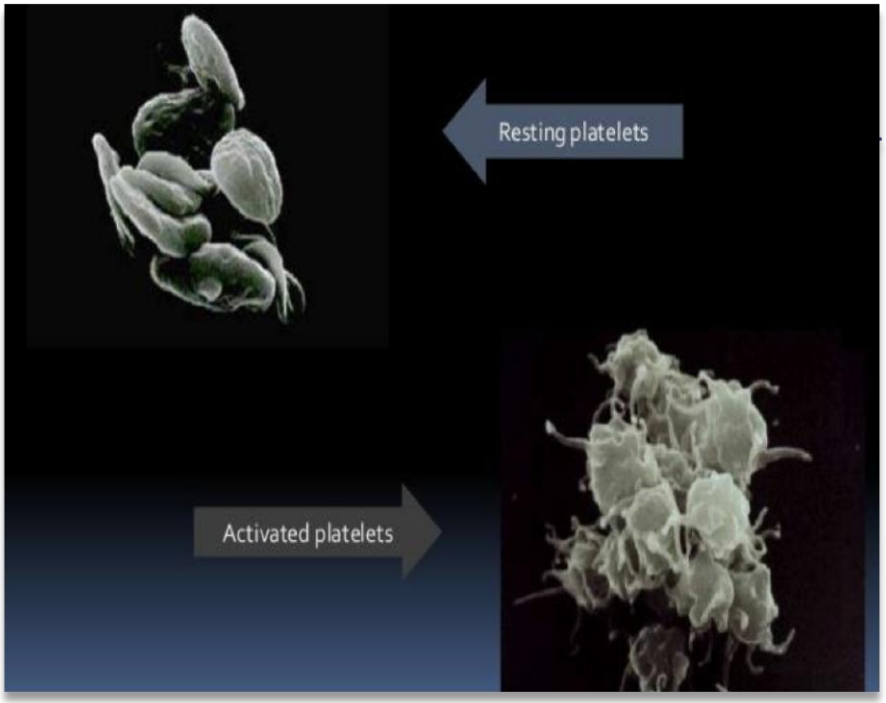
Platelet Functions

Platelet Functions in hemostasis Begins with (Platelet activation)



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

video

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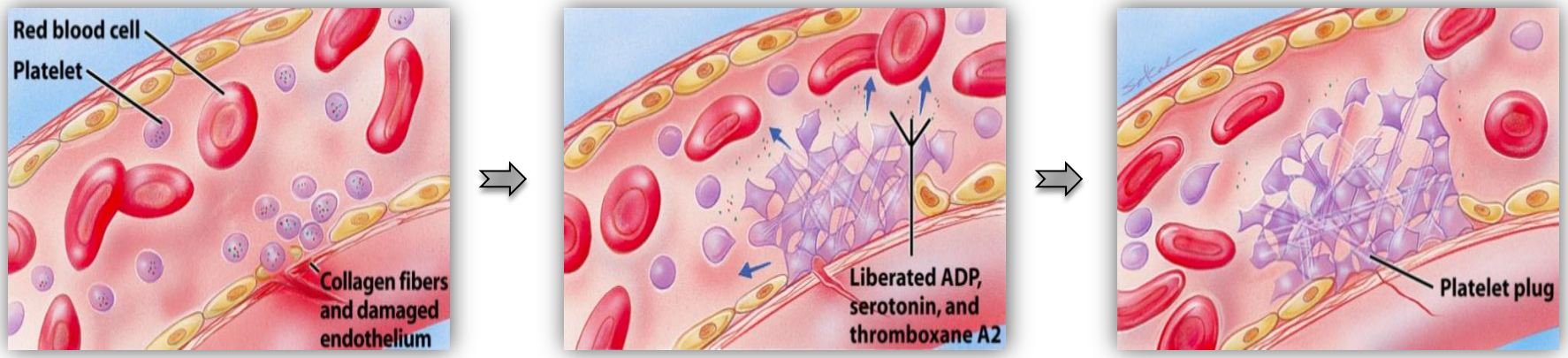
Steps of Platelet Activation

1. **Adhesion**
2. Shape change
3. **Release** "ADP , TXA2"
4. **Aggregation**
5. **Clot Retraction**



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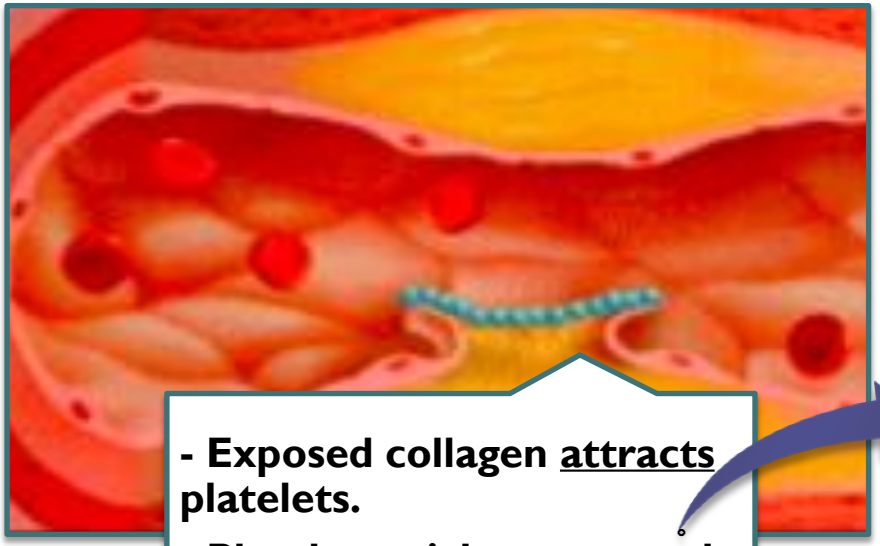
Platelet Adhesion

Adhesion : adhere platelets with collagen or sub endothelial tissue of the vessel wall.



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

smooth : Endothelial surface طالما إن الـ
بالتالي لا يوجد أي تجاذب بين
الـ Platelets والـ Endothelial cells
أي أن بينهما تنافر(They repel each other)

طبقة الـ Endothelial cells تختفي وتتبقى طبقة
الكولاجين التي تتميز بمقدرتها على جذب الـ Platelets

platelets ← Endothelial cell injured
will come and adhere to collagen, they
become sticky "like a gum".

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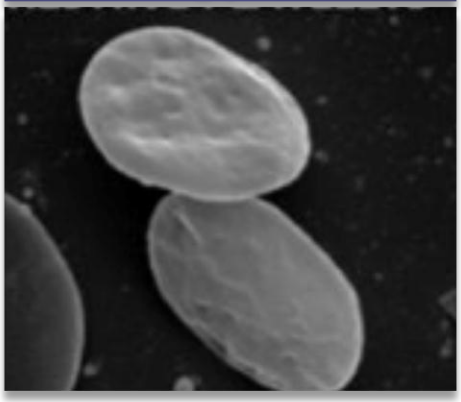
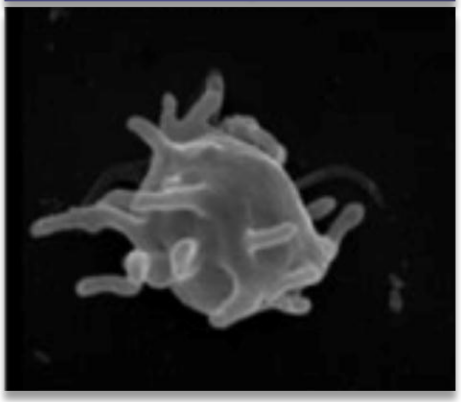
Platelet shape change

Resting platelets	Activated platelets
	

Platelet Activation means changing in platelet shape to form the plug

When platelets come in contact with damaged vascular surface , especially collagen fibers they immediately change their shapes into globular disc and they begin to swell , they form irregular shape with protruding from their pores

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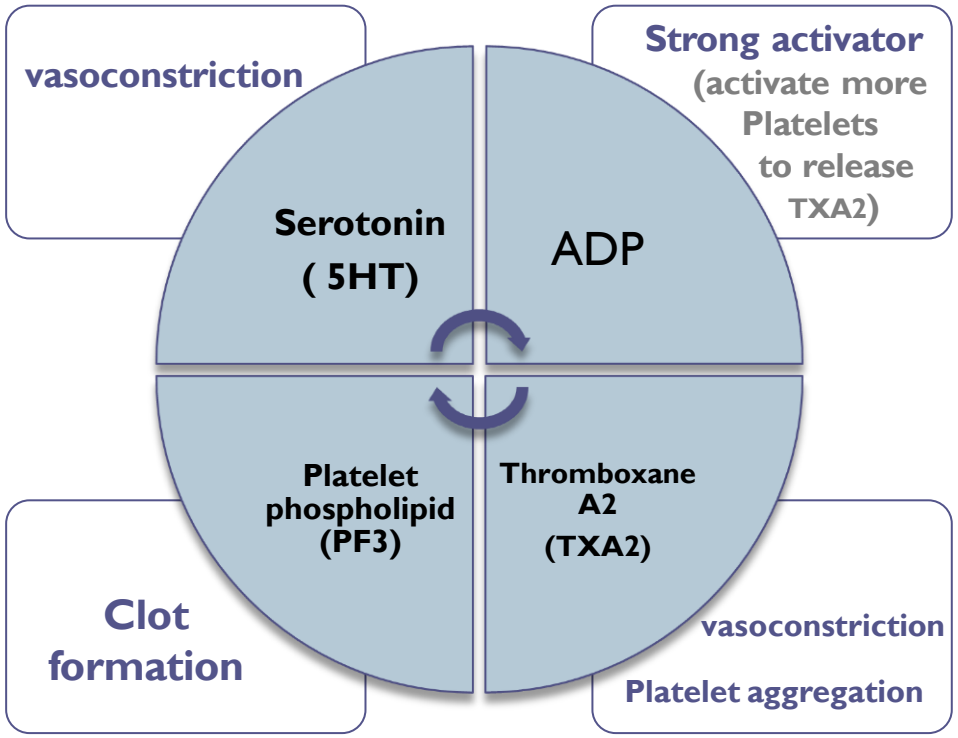
Platelet Release Reaction



-TXA2 is a prostaglandin formed from arachidonic acid
-TXA2 inhibited by Aspirin

يمنع تكون الجلطات لمقدرته على جعل الدم في حالة سائلة

ADP & Thromboxane A2 increase the stickiness of platelet

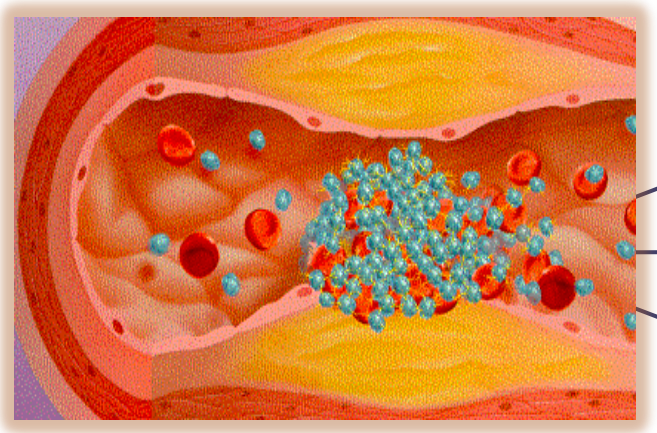
increase Platelets aggregation

plugging of the cut vessel

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

Thromboxane A2 exist in the cell membrane of platelets , NOT in in the granules.
TXA2 is prostaglandin formed from AA "arachidonic acid".

Platelet Aggregation



Aggregation:
adhering one platelet with other one

Activated platelets stick together and activate platelet to form a mass called a platelet plug

Plug reinforced by fibrin threads formed during clotting process

Aggregation = Interaction between platelets and other platelets. (many layers of platelets)

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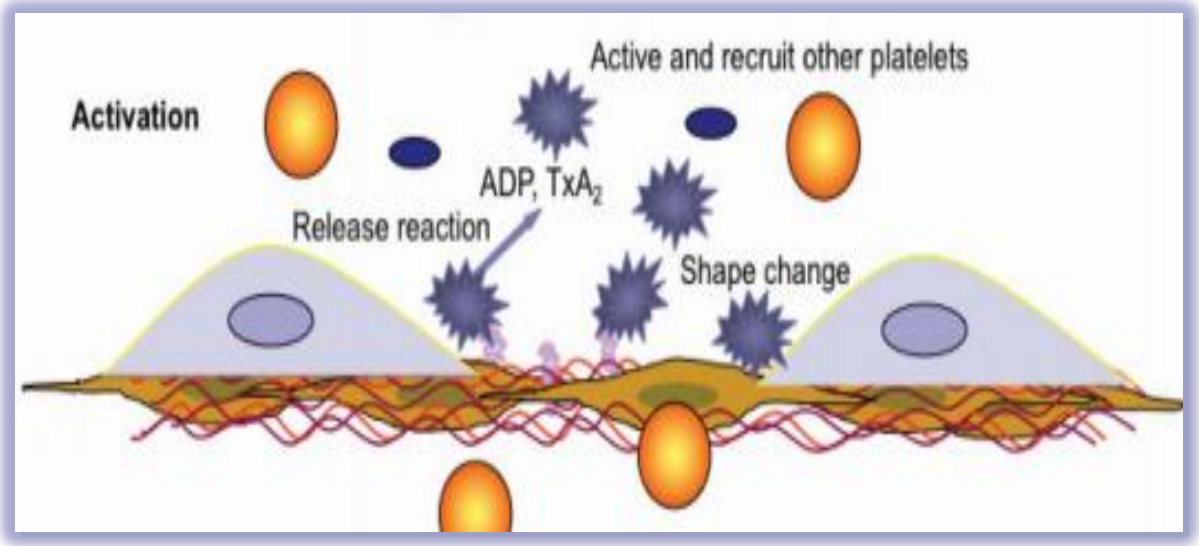
Clot Retraction



Myosin and actin filaments in platelets are stimulated to contract during Aggregation further reinforcing the plug and help release of granule contents.

Activation of clotting system → Fibrin which lead to SECONDARY hemostatic plug
(secondary = primary + Fibrin) كأنها ضماد أو شبكة تتكون فوق الصفائح الدموية لتحميها

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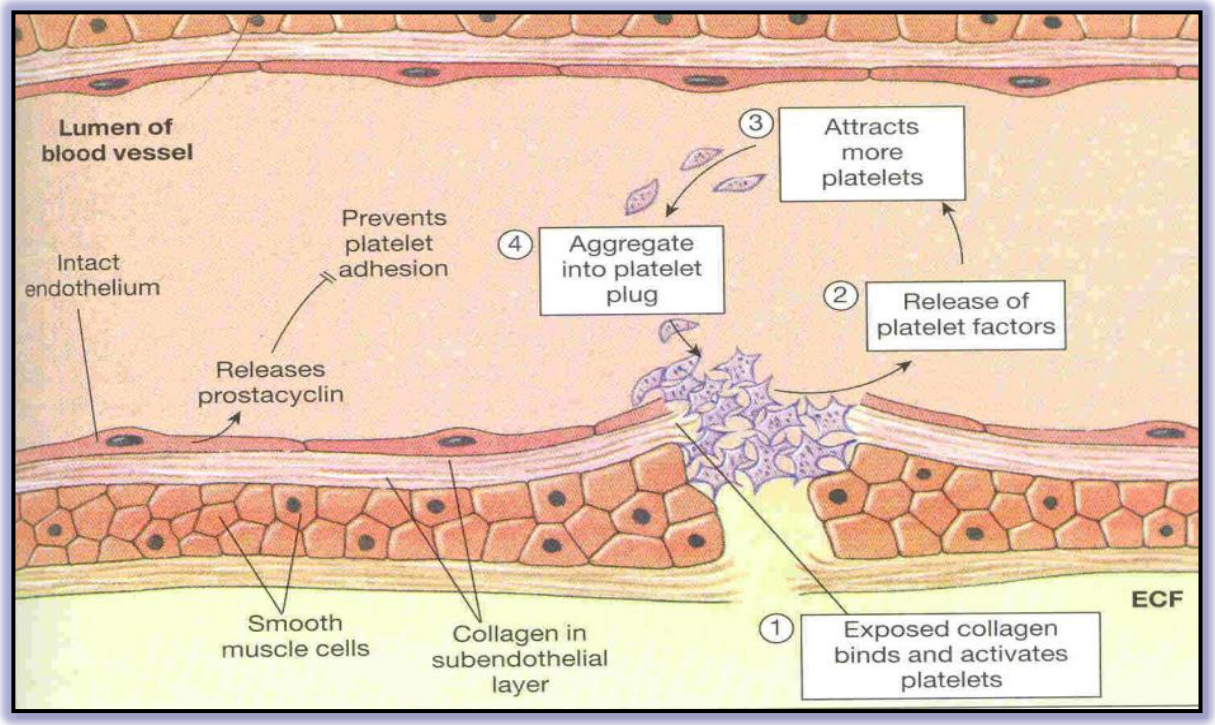
Platelet plug formation

اختصار تكوين هذه الطبقة : أولاً يرتبط الكولاجين بالصفائح ويعمل على تنشيطها وتغيير شكلها ، بالتالي بعدما تتنشط تفرز مكوناتها التي تعمل على جذب الصفائح الدموية الأخرى ، وأخيراً تتراكم الصفائح وتصنع طبقة تعمل على إغلاق مكان الإصابة.



- **(Bleeding) → (vasoconstriction) → (PRIMARY hemostatic plug) which involves :**
  Adhesion \ shape change \ release \ aggregation \ clot reaction
- **Activation of clotting system → Fibrin which lead to SECONDARY hemostatic plug**
  (secondary = primary + Fibrin) كأنها ضماد أو شبكة تتكون فوق الصفائح الدموية لتحميها

Video

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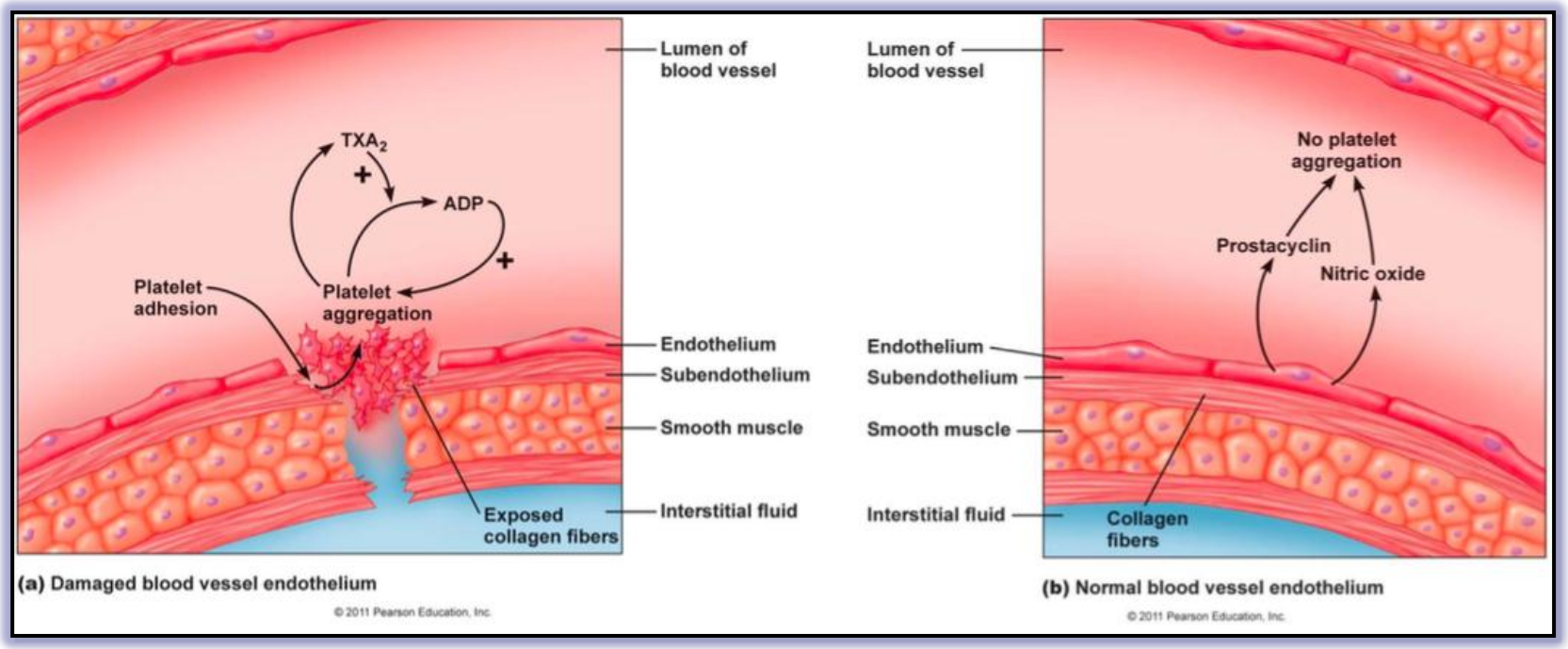
Platelet plug formation



Prostacyclin is one kind of prostaglandin

Importance of platelet plug for small vascular damage

Why the platelets plug is limited to the site of injury ? Healthy smooth Endothelial produce **Nitric oxide (No)** + **PGI2** (Prostacyclin) → **Vasodilation** and **inhibit aggregation** so that will prevents the formation of platelets **" no clot "** while the damaged endothelium secrets **ADP** and **TXA2** for clot bleeding

Video

"Start at 4:14"

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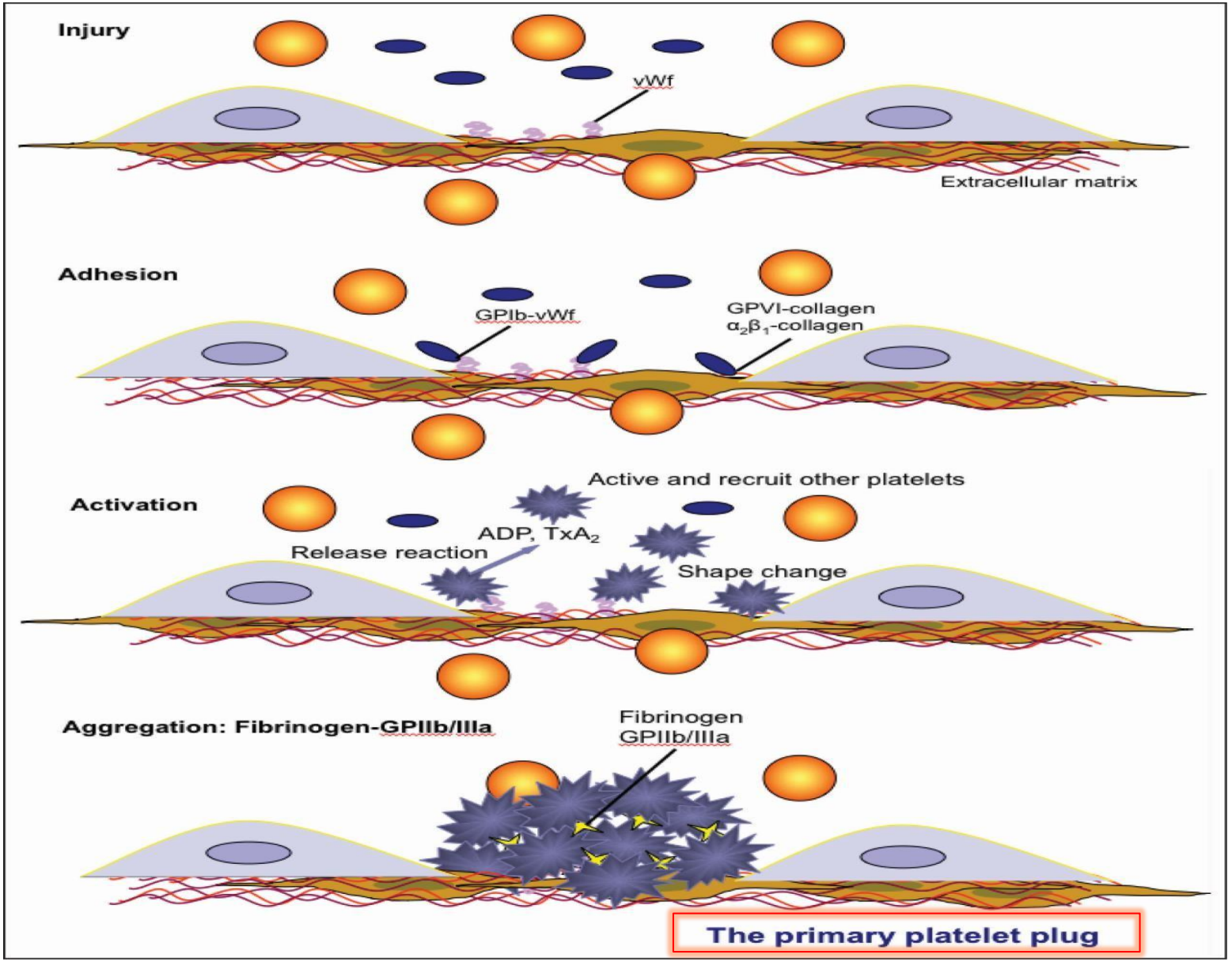
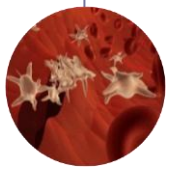
Review of the steps



Hemostatic mechanisms


Vessel wall


platelets


blood coagulation


Fibinolytic system

Synonyms		Clotting factor	
1	I	Fibrinogen	★
2	II	Prothrombin	★
3	III	Thromboplastin	
4	IV	Calcium	
5	V	Labile factor	
7	VII	Stable factor	
8	VIII	Antihemophilic factor A	★
9	IX	Antihemophilic factor B	★
10	X	Stuart-Power factor	
11	XI	Plasma thromboplastin antecedent (PTA)	
12	XII	Hagman factor	★
13	XIII	Fibrin stabilizing factor	★

memorize only what is marked with star

Clotting factors : Circulate in plasma in inactive sate , and soluble .

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General Explanation of the whole process "Overview"

- Coagulation system is series of events of chemical reactions.
- Coagulation system is composed of Extrinsic & Intrinsic pathways.
- Plug + Fibrin = Secondary hemostatic plug.
- (Fibrin = clot)
- Secondary hemostatic plug is stronger than primary one because of the presence of Fibrin + Activation of Intrinsic & Extrinsic pathways.
- We have 13 Coagulation factors.
- These factors activate only when injury occurs.
- Intrinsic pathway = داخلي / Extrinsic = خارجي

Coagulation cascade : series of biochemical reactions leading to the formation of blood clot.

Thrombin شبهه العلماء بالشلال لأن الشلال يكون قوياً في نهايته، فالموجود في النهاية هو
الذي يبدأ بكميات قليلة ثم يزداد بالتدريج.

- The importance of platelets :

Release of phospholipids (PFP) للخارج

ما هو الغرض ؟ إن التفاعلات تتم على سطح الصفائح الدموية

- الدم لديه خاصية مميزة وهي القدرة على الرجوع إلى الحالة الصلبة
- الصفائح الدموية تشارك في الخطوة الأولى :

Release of serotonin & Thromboxane A2 :Vasoconstriction.

وكذلك الخطوة الأخيرة :

Release of phospholipids + activation of factors + activation of protein (Fibrinogen)

- Fibrin يُفرز من الكبد ولكنه موجود أيضاً داخل الصفائح الدموية ، تستخدمها لتكوين الـ Fibrinogen

شرح لأهم المفاهيم بصورة عامة لتوضيح الفكرة فقط

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Intrinsic & Extrinsic

- Intrinsic :

السبب وراء تسميته بهذا الاسم أن العلماء قاموا بأخذ عينة دم ووضعوها في أنبوب ولاحظوا بعد فترة وجيزة تكون التجلط على نفس العينة فاستنتجوا أن كل العوامل التي يحتاجها الدم ليكون هذا التجلط أو التخثر موجودة داخل هذه العينة.

- Extrinsic :

سبب التسمية : أن هنالك عالم قام بأخذ عينة من دماغ فأر ثم أضافها إلى عينة دم سائلة (لاحتوائه على مادة الستريت التي ترتبط مع الكالسيوم (الكالسيوم هو الذي يساعد على تجلط الدم والأشخاص الذين يعانون من نقص في الكالسيوم معرضون للوفاة في حالات النزيف) ، الدم بقي على حالته السائلة بعد ذلك قام العالم بإضافة جزء من مخ الفأر على هذه العينة وتفاجأ أن الدم تخثر مما يعني أن هنالك عوامل خارجية من الممكن أن تنشط تجلط الدم.

للاستزادة فقط

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Blood coagulation

- This reactions activate prothrombine (inactive form) to Thrombin (active form) enzyme.
- Thrombin will change Fibrinogen (plasma protein) to Fibrin (insoluble protein).
- Prothrombin (inactive thrombin) is activated by a long Intrinsic or short Extrinsic pathways.
- Begins to develop in :
  - 15-20 sec → Minor trauma.
  - 1-2 min → Severe trauma.

Blood coagulation :

a series of biochemical reactions leading to the formation of blood clot.

هنالك بروتينات موجودة في الدم ولكنها في حالة غير نشطة منها بروتينات نطلق عليها :
"Coagulation factors " which circulate in blood in inactive form
أحدها يسمى Fibrinogenوهو بالإضافة إلى أنه غير نشط يعتبر ذائب في البلازما : "Fibrinogen is Soluble in plasma"
Injury ⟶ rupture of endothelial cells ⟶ activation of Fibrinogen ⟶ Fibrin.
Fibrin ناتج عن تحول الـFibrinogen الموجود في الدم ، كيف تحول إلى هذه الصورة ؟ عن طريق إنزيم مهم جداً يسمى :
Thrombin ناتج عن تنشيط الـ Coagulation system

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Blood coagulation (Thrombin)

Thrombin functions :
1- Activation of Fibrinogen to Fibrin.
2- Activation of Factor 13 "الصمغ".
3-Activation of Factor 5.
:Thrombin
كأنه يسوي تنشيط لنفسه فتزيد كميته وبالتالي يؤدي إلى تنشيط
ثم : الـ Platelets
Morphological changes that stimulate the release of ADP & Thromboxane A2.

Thrombin

Thrombin is essential in platelet morphological changes to form primary plug.

Activates Factor V "5"

Thrombin changes Fibrinogen to Fibrin.

Thrombin stimulates platelets to release ADP & thromboxane A2; both stimulate further platelets aggregation

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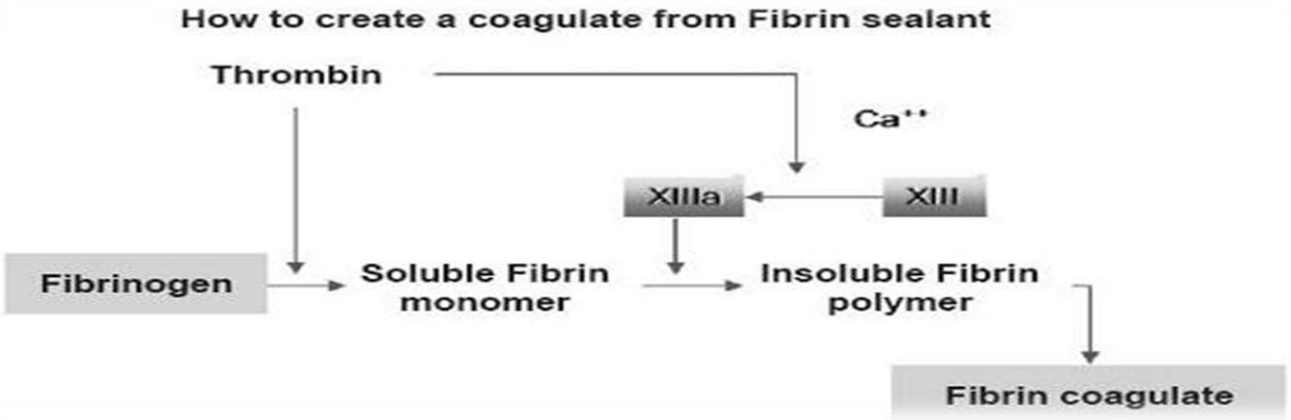
Blood coagulation



Click on the underlined word for further information

- Factor XIII (13) is activated by thrombin into factor XIIIa
- its activation into Factor XIIIa requires calcium as a cofactor
- XIIIa acts on fibrin to form amide cross links between fibrin molecules to form an insoluble clot.

In other words:

- Fibrin is the main protein constituent of the blood clot, which is stabilized by factor XIIIa through an amide or isopeptide bond that binds adjacent fibrin monomers

كيف يصير الـFibrin صلب وغير ذائب ؟

Fibrinogen has 2 ends , Fibrino peptide A&B ,Thrombin will removes these 2 ends and give rise to Fibrin monomers (A&B ends لكن بدون Fibrin عبارة عن)

لما تنشال هذي النهايات ، الـ Fibrin monomers راح تتجمع لكنها تحتاج مساعدة، مين اللي يساعدها ؟

(Factor 13) :

Fibrin polymer مع بعضها بالتالي يتكون Fibrin monomers مثل الصمغ ، يلصق الـ

Fibrin polymer is stronger and more stable.

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Intrinsic pathway

- **The trigger is the activation of factor XII(12) by contact with foreign surface, injured blood vessel, and glass.**

- **XII ⟹ XIIa (XIIa + HMW kininogen + Prekallikrein) ⟹ XI**
- **XI ⟹ XIa (XIa + Ca) ⟹ IX**
- **IX ⟹ IXa (IXa + VIII + Platelet phospholipid + Ca) ⟹ X**
- **X ⟹ Xa (Xa + V + Platelets+ Ca) ⟹ Thrombin**
- **Thrombin (leads to transformation of) : Fibrinogen ⟹ Fibrin**

(Factor 12) is called as " Contact Factor " because it contacts with collagen or subendothelial tissue and become Active.

- Activation will start from (Factor 12)which activate (Factor 11) by the help of high molecular weight kininogen prekallikrein (that will accelerate the reaction).
- Active (Factor11) will activate (Factor 9) Active (Factor 9) في وجود الكالسيوم
- Active (Factor 9) activate (Factor 10) في وجود :
  Platelets & (Factor 8) & calcium
- (Factor 8) :
  Platelets & Calcium : في وجود "Cofactor» يعمل كإنزيم يسرع العملية
- Platelets & (Factor 5) & Calcium: في وجود :

Active (Factor 10) will activate Prothrombin (Factor 2) which is then transform into Thrombin.

- Thrombin : will change Fibrinogen into Fibrin (Blood clot).
- Fibrinogen is (soluble in plasma) while Fibrin is (Insoluble) that's why it forms the blood clot.
- A (الموجود بجوار الأرقام) means "Active".

شرح للمخطوطات السابقة

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Extrinsic pathway

- Triggered by material released from damaged tissues (tissue Thromboplastin "TF")
- Tissue Thromboplastin "TF" + VIIa + Ca ⟹ Xa
- Xa + V + Platelet phospholipid "PF3" + Ca (prothrombin activator) it is a proteolytic enzyme activate prothrombin ⟹ Thrombin
- Thrombin act on fibrinogen : Fibrinogen ⟹ Fibrin "insoluble thread".
- Factor XIII (13) + Ca ⟹ strong fibrin (strong clot)

- Starts from :Tissue Factor (TF) which is a Lipoprotein arise from injured endothelial cells " Injured tissue ⟶ Tissue Factor (TF) "
- Tissue Factor will activate (Factor 7).

في وجود الكالسيوم :

(Factor 7) will activate (Factor 10) which converts Prothrombin into Thrombin.

- Thrombin : Fibrinogen ⟶ Fibrin ⟶ Blood clot

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TF = also called tissue factor

Xa (10) + V, Ca,
phospholipid from platelets

Prothrombin (II)

Thrombin (IIa)

Fibrinogen (I)

Fibrin (soluble) $\xrightarrow{\text{XIII, Ca}}$ insoluble fibrin

Common pathway
الخطوات المشتركة بين المسارين

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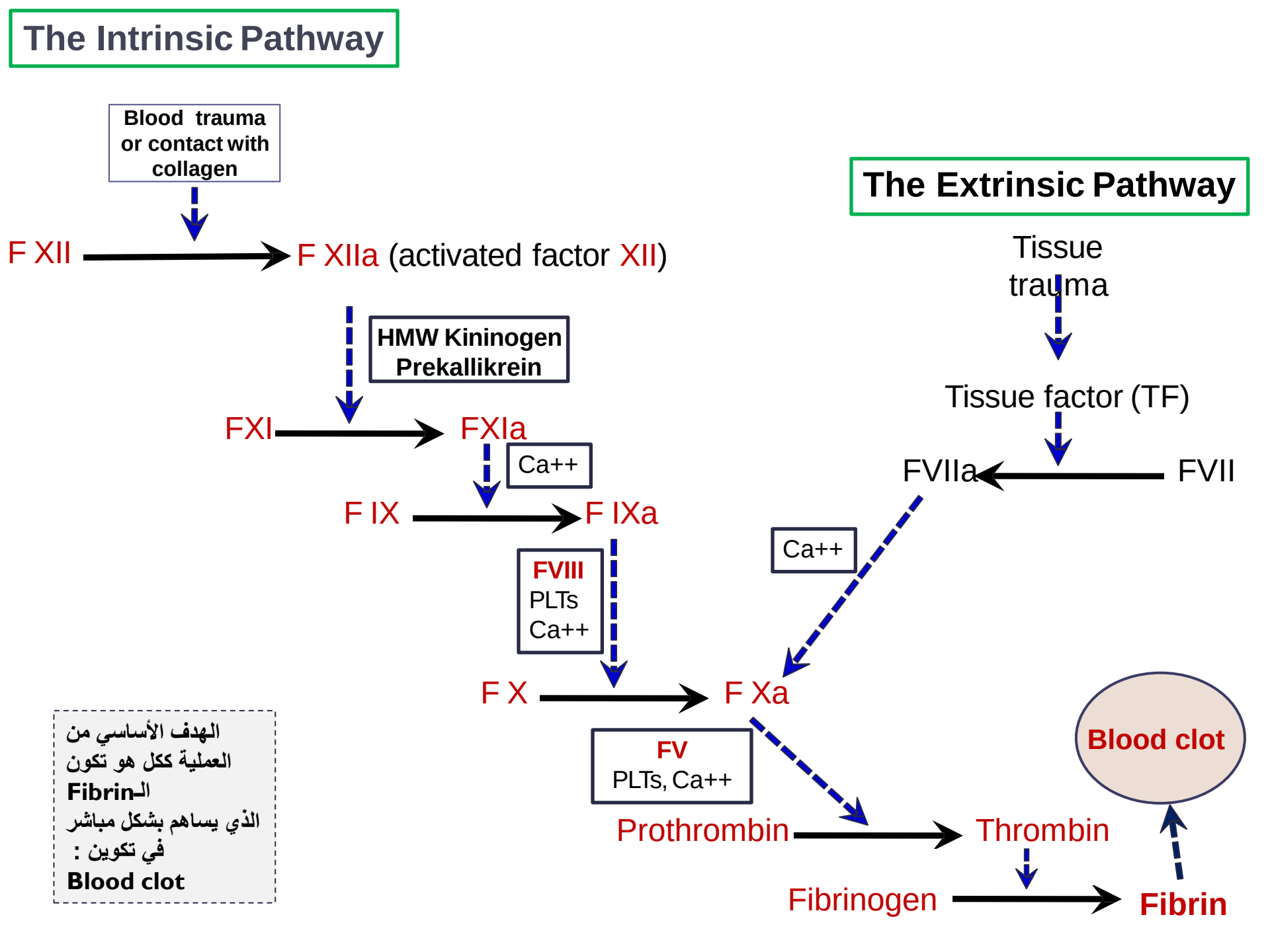
The Intrinsic Pathway
Blood trauma or contact with collagen
F XII
F XIIa (activated factor XII)
HMW Kininogen Prekallikrein
FXI
FXIa
Ca++
F IX
F IXa
FVIII
PLTs
Ca++
F X
F Xa
FV
PLTs, Ca++
Prothrombin
Thrombin
Fibrinogen
Fibrin
Blood clot
The Extrinsic Pathway
Tissue trauma
Tissue factor (TF)
FVIIa
FVII
Ca++
الهدف الأساسي من العملية ككل هو تكون الـFibrin الذي يساهم بشكل مباشر في تكوين :
Blood clot

Activation blood coagulation

- **Intrinsic pathway:**
  All clotting factors present in the blood.

- **Extrinsic pathway:**
  Triggered by tissue factor.

(مهم)

-Intrinsic is LONGER than Extrinsic pathway , Extrinsic pathway is FASTER & SHORTER.

-Both will be stimulated at the SAME TIME.

وجه الشبه بين Extrinsic & Intrinsic Pathway :

Both will activate (Factor 10) and the result is the formation of Thrombin which then converts Fibrinogen into Fibrin.

وجه الاختلاف:

Intrinsic is long while Extrinsic is short.

video

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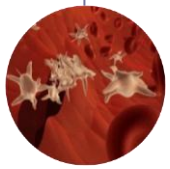
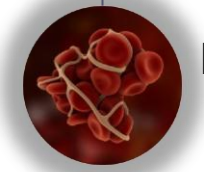
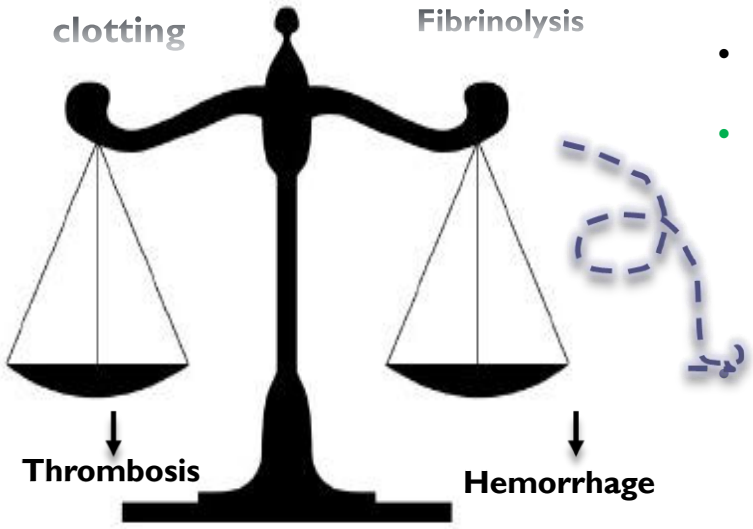
Hemostatic mechanisms


Vessel wall


platelets


blood coagulation


Fibinolytic system



- **Formed blood clot can either become fibrous or dissolve.**
- **Fibrinolysis (dissolving) = Break down of fibrin by naturally occurring enzyme plasmin therefore prevent intravascular blocking.**

There is balance between clotting and fibrinolysis.

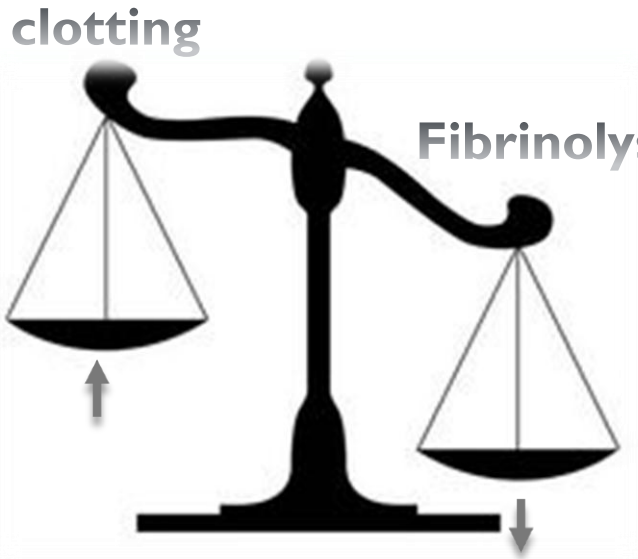
- Excess fibrinolysis leads to tendency for bleeding

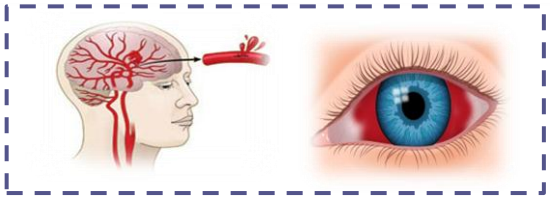
-Excess clotting leads to Blocking of blood vessels

انتهت المهمة وتوقف النزيف ، يبدأ الجسم يحلل التجلط عشان ما يكبر ويسبب مشاكل مثل تصلب الشرايين والجلطات ، الإنزيم المهم جداً هنا هو :
Plasmin which breakdown Fibrin into Fibrin degradation products (FDPs).

imbalance between clotting and fibrinolysis

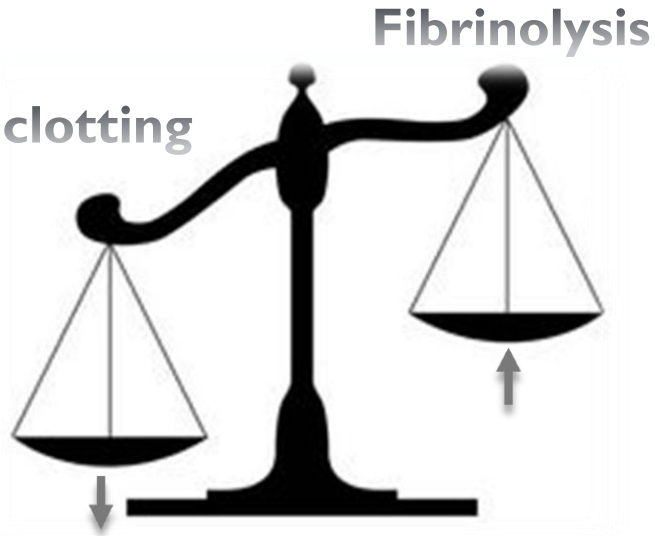
Hemorrhage

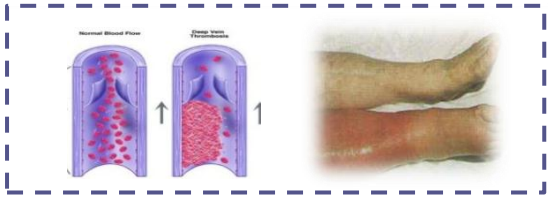




Video

Thrombosis





Video

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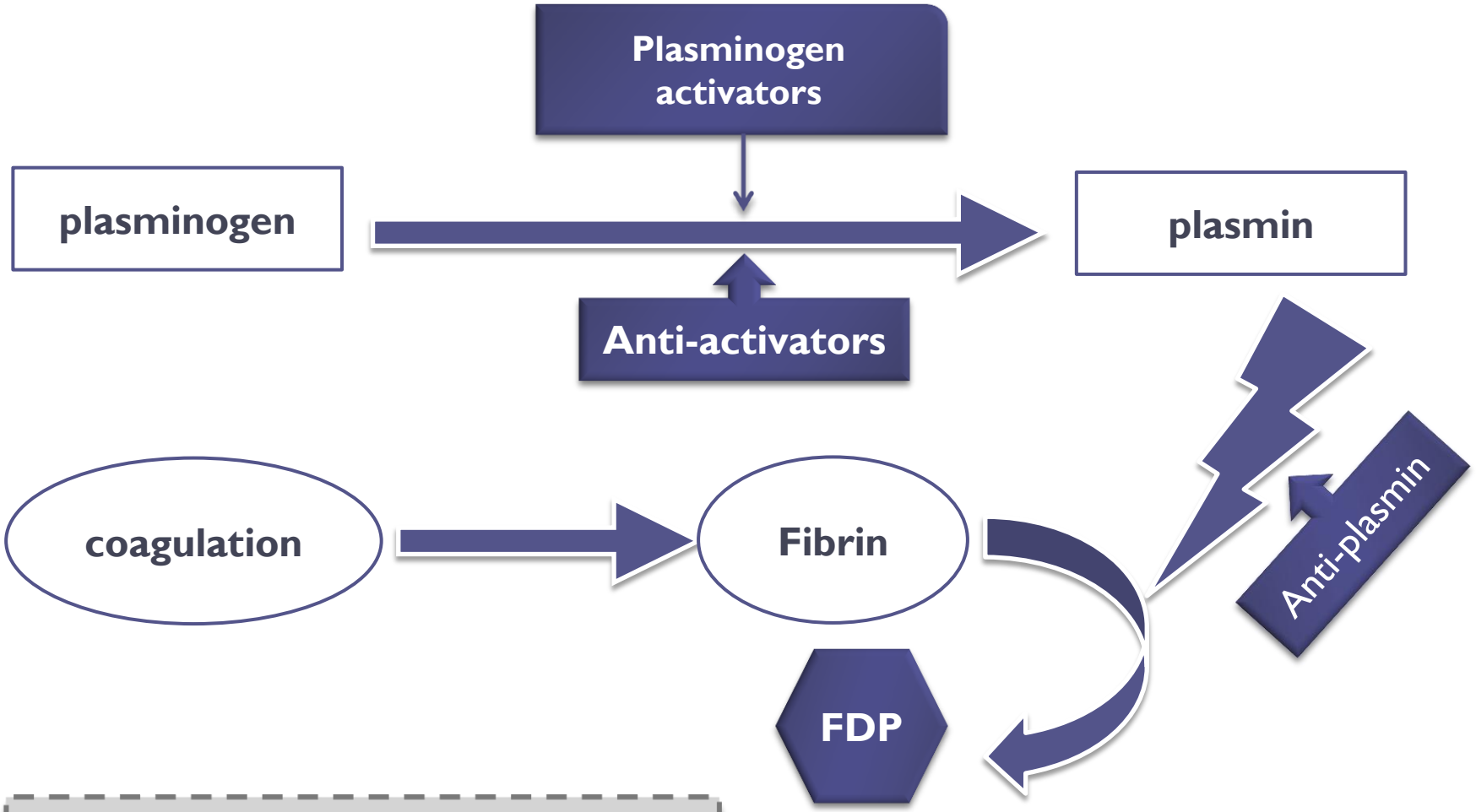
لازم يكون فيه توازن بين التخثر والتحلل

The fibrinolysis System



FDP : Fibrin Degradation Products

Video

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plasmin

- Plasminogen (exist in blood in inactive form) transformed into plasmin by Tissue plasminogen Activator (TPA)

- TPA arise from endothelial cells.

- Plasmin —يكسر→ Fibrin —إلى→ Fibrin Degradation Products (FDP)

Fibrin

Fibrin degradation product (FDP)

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Plasmin

Plasmin

Unwanted effect of plasmin : is the digestion of clotting factors.

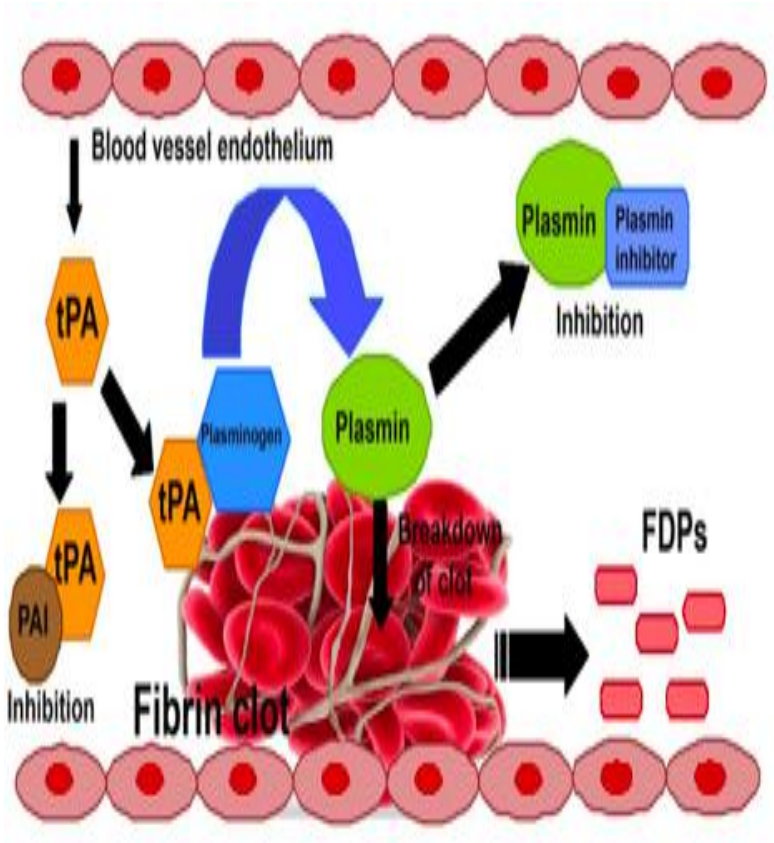
Plasmin is activated by : tissue plasminogen activators (t-PA) in blood.

Plasmin is controlled by: - Plasminogen Activator Inhibitor (PAI) Anti-plasmin from the liver.

Plasmin is present in the blood in inactive form (Plasminogen).

Uses : Tissue Plasminogen activator (t-PA) used to activate plasminogen to dissolve coronary clots

Plasmin digest : intra & extra vascular deposit of Fibrin " Fibrin degradation products (FDP)".



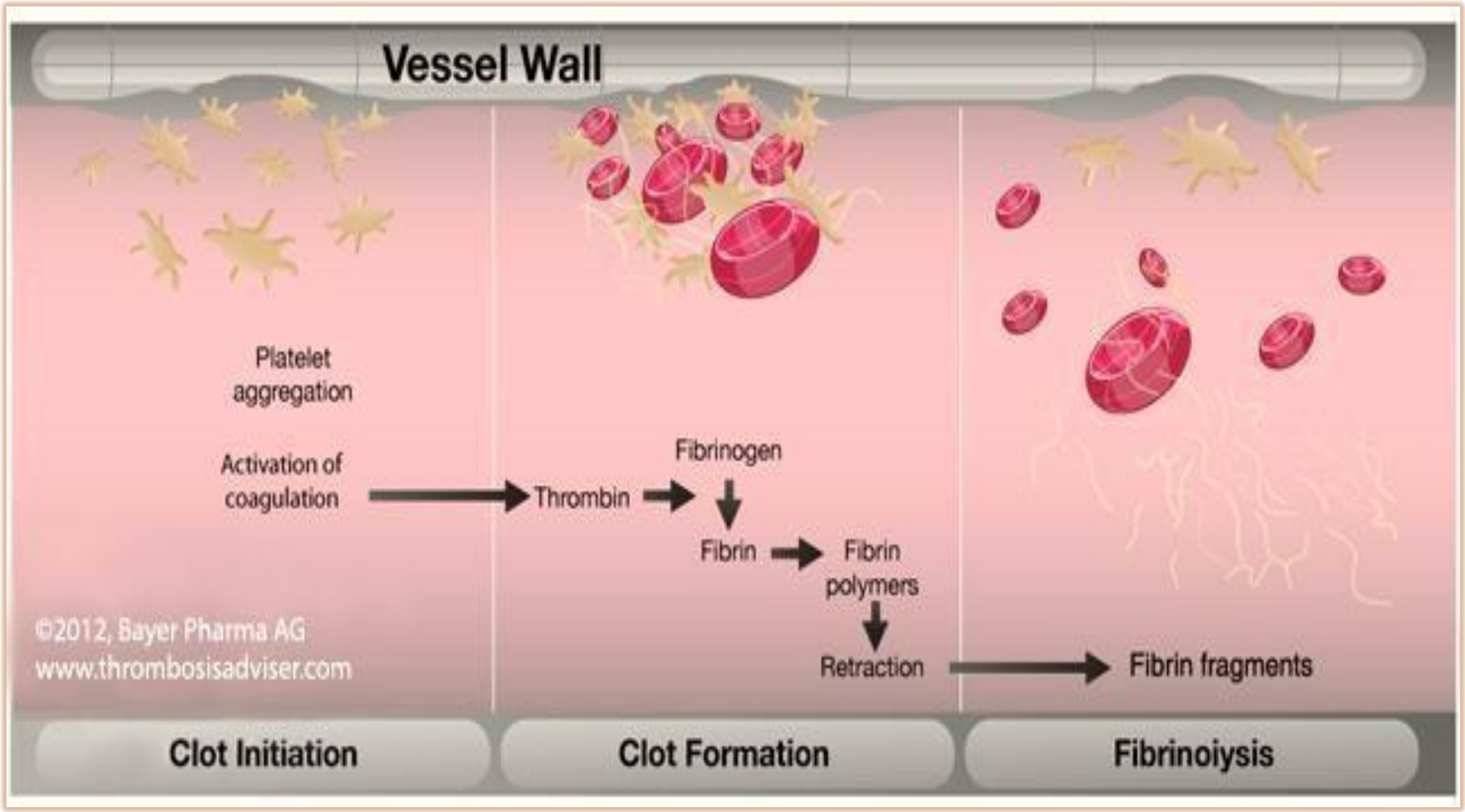
كل موظف عليه مدير يراقبه ، وبالمثل الـ Plasmin و الـ TPA عليهم مدير يراقبهم

- Plasminogen activator inhibitor (PAI) that inhibit TPA
- Anti-plasmin will inhibit Plasmin
- Control of Fibrinolysis :

1. PAI : inhibit TPA / 2. Anti-plasmin : inhibit plasmin

لو عندنا مريض مصاب بجلطة وجاء للمستشفى خلال وقت قصير يعطى مباشرة مادة تقوم بتحليل هذا التجلط ، هذه المادة هي نفسها الـTPA تقوم بتحليل الجلطة وتكسيرها.

Hemostasis Mechanism



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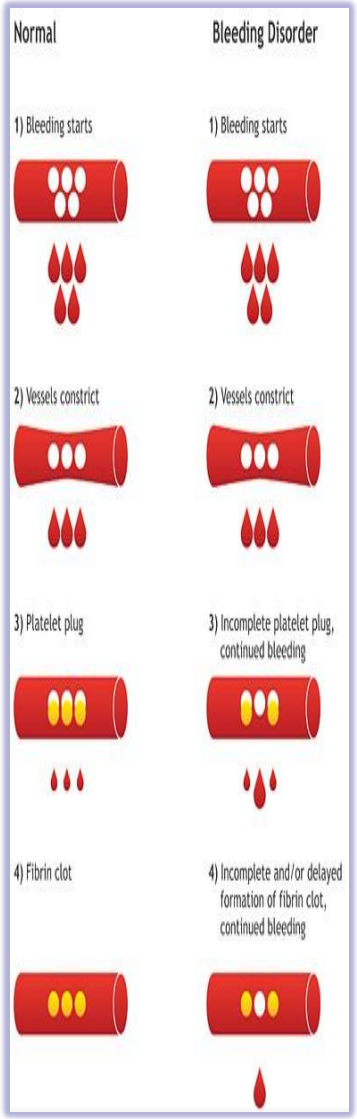
Bleeding disorders



Hemophilia:

Increase bleeding tendency.

X-linked disease.

Affects males.

85% due to FVIII deficiency

(hemophilia A) , and 15% due to FIX deficiency

(hemophilia B).

"A disorder in which blood doesn't clot normally."

Vitamins K deficiency & liver disease:

Almost all coagulation factors are synthesized in the liver.

Prothrombin, FVII , FIX , FX require vitamin K for their synthesis

Platelet defects:

Deficiency in number : (thrombocytopenia) or defect in function

"Normal platelets, they just can't do their function"

Vitamin K : مهم لتصنيع ٤ عوامل مهمة جداً ونقصها يؤدي إلى نزيف
٢ و ٧ و ٩ و ١٠ : "١٩٧٢" > to memorize them
Abnormalities of hemostasis :
Abnormality affecting platelets > No efficient platelets formation.
Thrombocytopenia " less number of platelets".
Abnormality affecting the function of platelets > Bleeding.
Deficiency of factor 8 > Hemophilia.

Hemophilia A & B, Vitamin K Deficiency

Hemophilia A vs B

Mind Map

Note : * use this mind map for revision not studying cuz not all the info included!

A

Hemostasis: the spontaneous arrest of bleeding from ruptured blood vessels

Mechanisms:

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

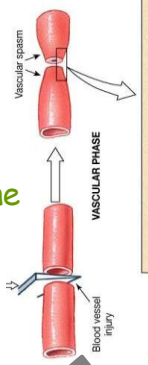
Hemostatic Mechanisms

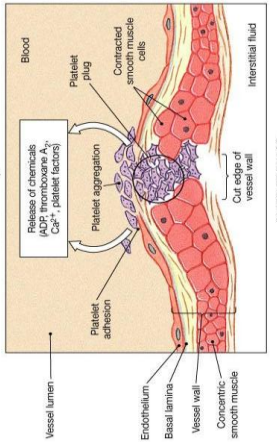
1. Vessel wall

Immediately After injury a localized Vasoconstriction

Mechanism:

- Systemic release of adrenaline
- Nervous factors
- local release of thromboxane A2 & 5HT by platelets





Haemostasis

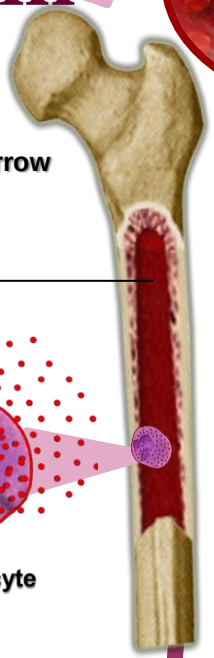
Platelets origin

Thrombocytes are Fragments of megakaryocytes in the bone marrow

Regulation of thrombopoiesis By:

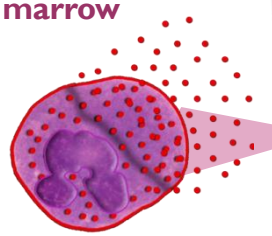
Thrombombopoietin

Site of formation : **Bone marrow**



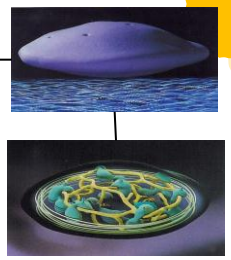
Steps:

Stem cell
↓
Megakaryoblast
↓
Megakaryocyte
↓
Platelets



Platelet Functions

Begins with Platelet activation



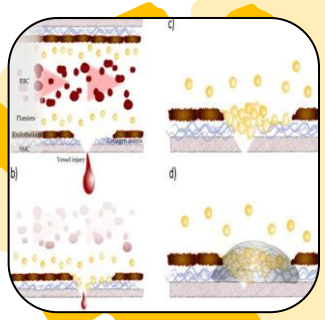
small disc shaped cells

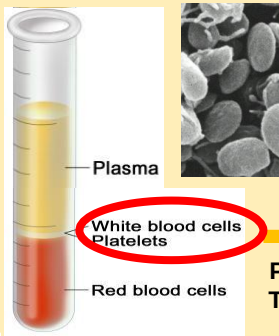
Platelet count = 150x10³-300x10³/ml,

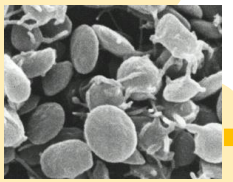
life span 8-12 days
Contain high calcium content & rich in ADP

Active cells contain contractile protein,

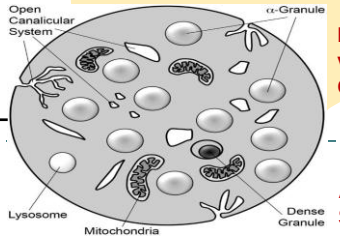
2. Platelet haemostatic plug formation







Platelets (PLT)
Thrombocytes



Fibrinogen
vWF
Other proteins

ADP
Serotonin Calcium

Mind Map

Note : * use this mind map for revision not studying cuz not all the info included! *

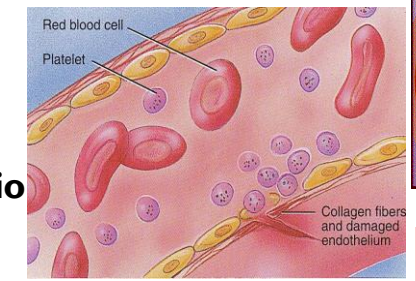
B

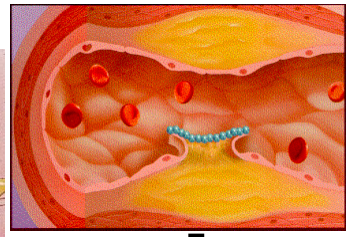
Platelets function begins with **Platelet Activation**

Platelet Activation

- Adhesion
- Shape change (activated)
- Aggregation
- Release (secretio
- Clot Retraction

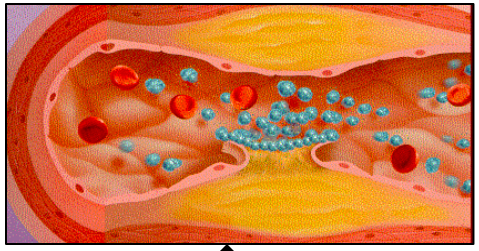
Platelet Adhesion





* Exposed **collagen** attracts platelets

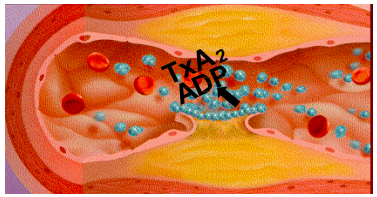
* Platelets stick to exposed collagen underlying damaged endothelial cells in vessel wall

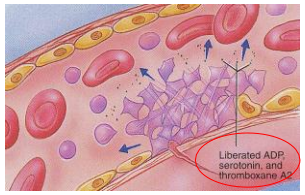


* Platelets activated by adhesion

*extend projections to make contact with each other

Platelet Release Reaction





Haemostasis

Activated platelets release Serotonin, ADP & Thromboxane A2

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

ADP & Thromboxane A2 (TXA2)→↑the stickiness of platelets →↑Platelets aggregation → plugging of the cut vessel

Resting **Activated**

Activated Platelets

Secrete:

1- 5HT → vasoconstriction

2- ADP

3- Platelet phospholipid (PF3) → clot formation

4- Thromboxane A2 (TXA2) is a prostaglandin formed from arachidonic acid

function:

Vasoconstriction

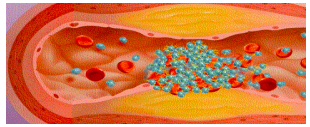
Platelet aggregation

(TXA2 inhibited by aspirin)

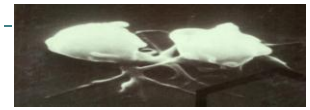
Platelets aggregation

* Activated platelets stick together and activate New platelets to form a mass called a platelet plug

* Plug reinforced by fibrin threads formed during clotting process



Platelet shape change and Aggregation



Mind Map

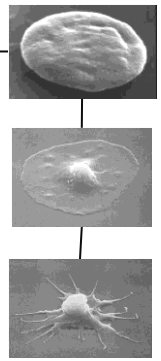
Note : * use this mind map for revision not studying cuz not all the info included! *

C

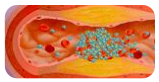
Platelets function begins with **Platelet Activation**

Platelet Activation

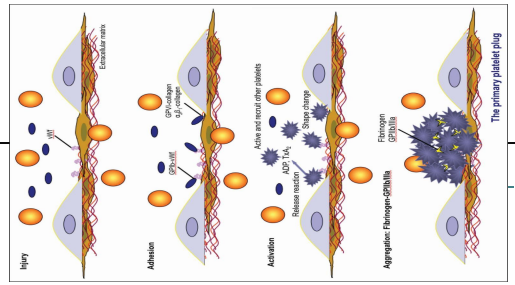
- **Adhesion**
- **Shape change (activated)**
- **Aggregation**
- **Release (secretion)**
- **Clot Retraction**



Clot Retraction:

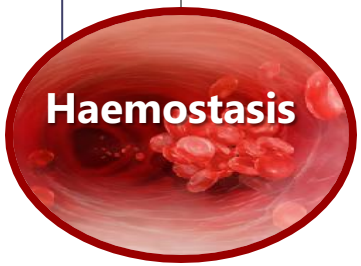


Myosin and actin filaments in platelets are stimulated to contract during aggregation further reinforcing the plug and help release of granule contents



Hemostatic Mechanisms

1- Vessel wall √
2- Platelet √
3- Blood coagulation
4- Fibrinolytic system



3. Blood coagulation (clot formation)

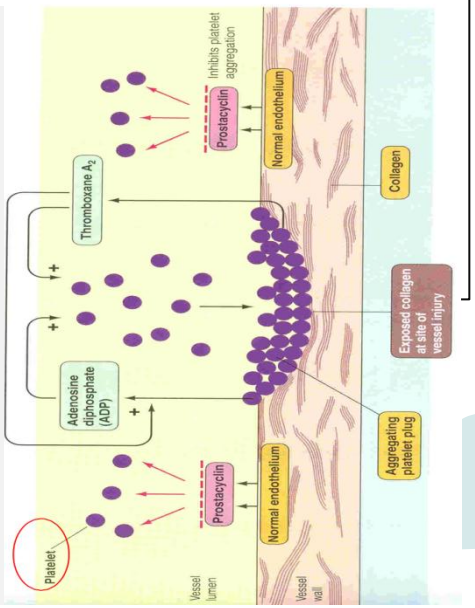
* A series of biochemical reactions leading to the formation of a blood clot

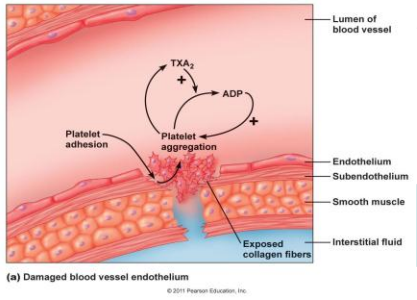
* This reaction leads to the activation of thrombin enzyme from inactive form prothrombin

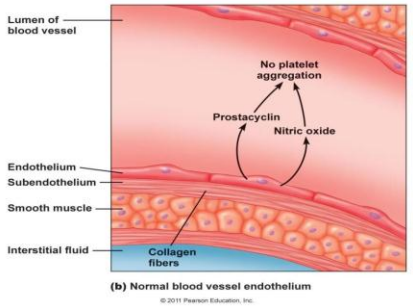
* Thrombin will change fibrinogen (plasma protein) to fibrin (insoluble protein)

* Prothrombin (inactive thrombin) is activated by a long intrinsic or short extrinsic pathways

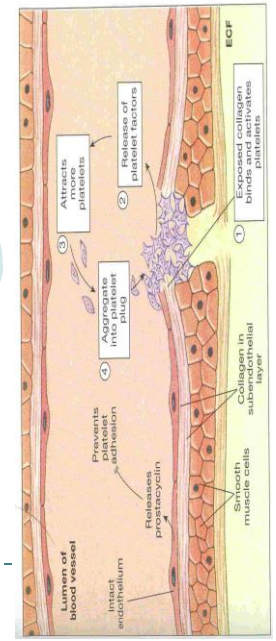
Intact endothelium secret prostacyclin and NO which inhibit aggregation







Platelet plug formation



Mind Map

Note :

- use this mind map for revision not studying cuz not all the info included!

D

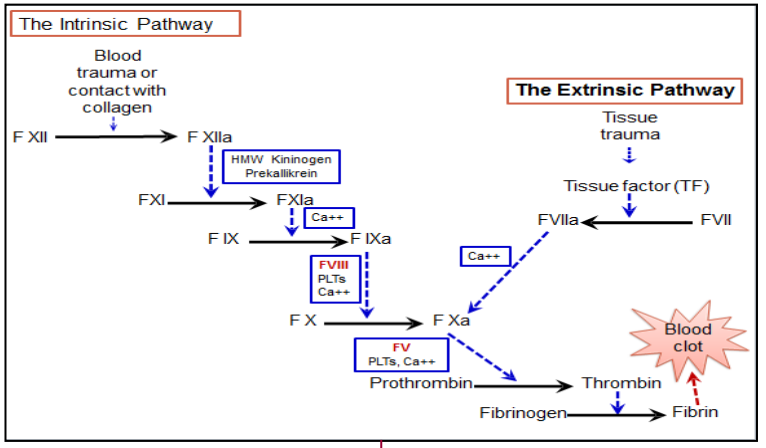
Hemostatic Mechanisms

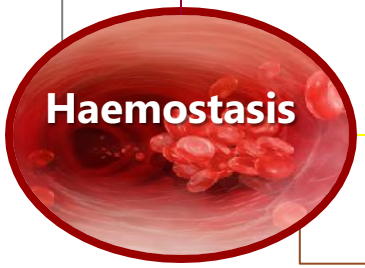
1- Vessel wall √
2- Platelet √
3- Blood coagulation
4- Fibrinolytic system

Clotting Factors

Circulate in plasma in inactive

Factors	Names
I	Fibrinogen
II	Prothrombin
III	Thromboplastin
IV	Calcium
V	Labile factor
VII	Stable factor
VIII	Antihemophilic factor A
IX	Antihemophilic factor B
X	Stuart-Power factor
XI	Plasma thromboplastin antecedent (PTA)
XII	Hagman factor
XIII	Fibrin stablizing factors





Intrinsic pathway

The trigger is the activation of factor XII by contact with foreign surface, injured blood vessel, and glass

Activate factor (XIIa) will activate XI

XIa will activate IX

IXa + VIII + platelet phospholipid + Ca activate X

Following this step the pathway is common for both

Extrinsic pathway

Triggered by material released from damaged tissues (tissue thromboplastin)

Tissue thromboplastin +VII+Ca→activateX Common pathway

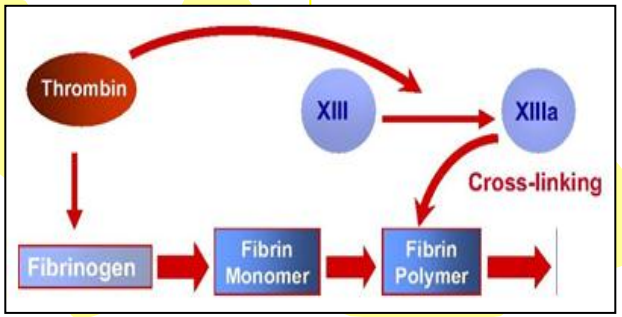
Thrombin act on fibrinogen →insoluble thread like fibrin

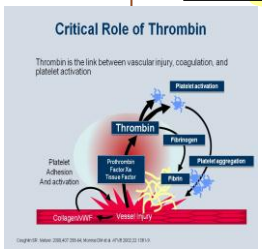
Factor XIII + Ca →strong fibrin (strong clot)

Intrinsic Pathway	Pathway Extrnsic
Contact activation ↓ XII →XIIa ↓ XI →XIa ↓ IX →IXa ↓VIII, Ca,P X →Xa	Tissue Factors ↓ ↓ ↓ ↓VII,Ca ↓ ↓ ↓ Xa ←X

Xa
↓
↓V, Ca, P
Prothrombin (II) →Thrombin (IIa)
↓
Fibrinogen (I) →Fibrin (soluble)
↓XIII, Ca
Insoluble fibrin

common pathway





Thrombin

Thrombin changes fibrinogen to fibrin

Activates factor V

Thrombin is essential in platelet morphological changes to form primary plug

Thrombin stimulates platelets to release ADP & thromboxane A2; both stimulate further platelets aggregation

Mind Map Note :

*** use this mind map for revision not studying cuz not all the info included!**

E

Activation Blood Coagulation

- Intrinsic Pathway: all clotting factors present in the blood
- Extrinsic Pathway: triggered by tissue factor

Common Pathway

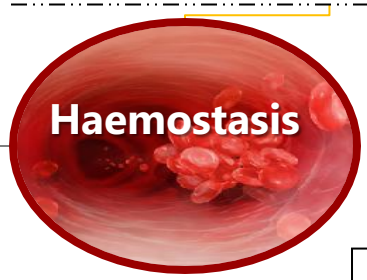
Intrinsic Pathway	Extrinsic pathway
Contact activation ↓ XII → XIIa ↓ XI → XIa ↓ IX → IXa ↓VIII, Ca,P* X → Xa	Tissue factor ↓ ↓VII,Ca ↓ Xa ← X
Xa ↓ ↓V, Ca, P* Prothrombin (II) → Thrombin (IIa) ↓ Fibrinogen (I) → Fibrin (soluble) ↓XIII, Ca insoluble fibrin	

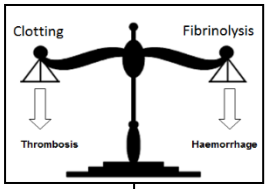
P* = phospholipid from platelets

Bleeding disorders

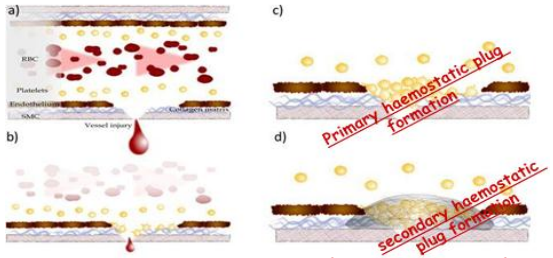
- Excessive bleeding can result from:
  - Platelet defects: deficiency in number (thrombocytopenia) or defect in function.
  - Coagulation factors defect:
    - Deficiency in coagulation factors (e.g. hemophilia)
    - Vitamin K deficiency.

- 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.





Platelet haemostatic plug formation



Hemostatic Mechanisms

1- Vessel wall √
2- Platelet √
3- Blood coagulation √
4- Fibrinolytic system

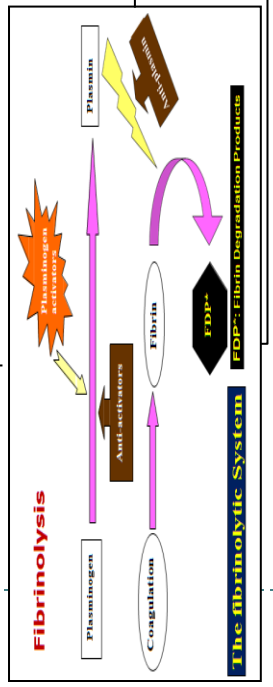
4. Fibrinolysis

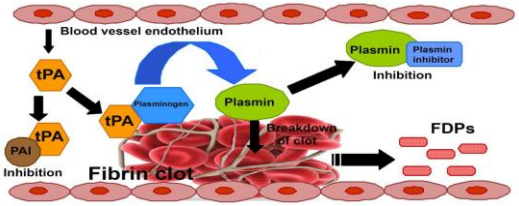
* Formed blood clot can either become fibrous or dissolve

* Fibrinolysis (dissolving) = Break down of fibrin by naturally occurring enzyme plasmin therefore prevent intravascular blocking

* There is balance between clotting and fibrinolysis

-Excess clotting →blocking of BloodVessels
-Excess fibrinolysis →tendency for bleeding





*Plasmin is present in the blood in inactive form Plasminogen

*Plasmin is activated by tissue plasminogen activators (t-PA) in blood.

*Plasmin digest intra & extra vascular deposit of Fibrin → fibrin degradation products (FDP)

*Unwanted effect of plasmin is the digestion of clotting factors

❖ **Plasmin is controlled by:**
- Plasminogen Activator Inhibitor (PAI)
- Antiplasmin from the liver

❖ **Uses:**

Tissue Plasminogen Activator (t-PA) used to activate plasminogen to dissolve coronary clots

Physiology team

QUIZ

خولة العماري
الهنوف الجلعود
إلهام الزهراني
رغد النفيسة
نورة القحطاني
منيرة الحسيني
منيرة السلولي
عريب العقيل
ملاك الشريف
منيال باوزير
فتون الصالح
أفنان المالكي
ربى السليمي

عمر العتيبي
رواف الرواف
حسن البلادي
عمر الشهري
عادل الشهري
عبدالله الجعفر
عبدالرحمن البركة
محمد الشيباني
خليل الدريبي
عبدالعزيز الحماد
عبدالعزيز الغنايم
عبدالمجيد العتيبي

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