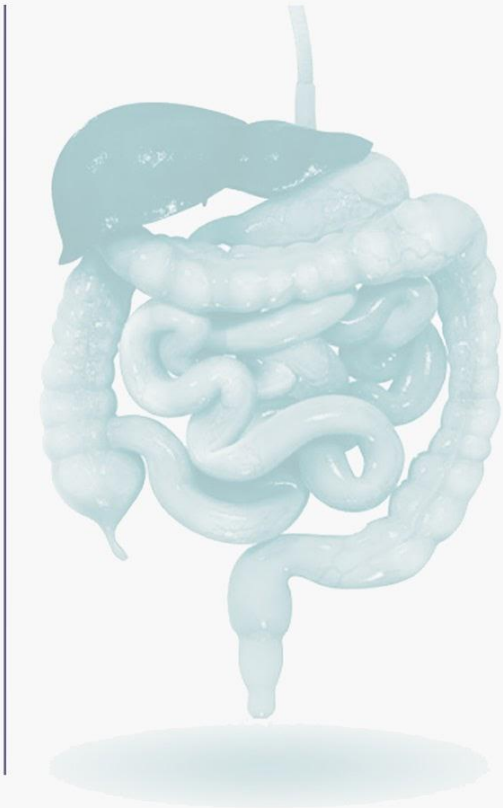
#9 Coagulation mechanism and Hypercoagulability



objectives :

- Recognize the different clotting factors
- Understand the role of calcium ions during clotting cascades.
- Describe the cascades of intrinsic and extrinsic pathways for clotting.
- Recognize process of fibrinolysis and function of plasmin
- Recognize some conditions causing excessive bleeding
- Understand some important anticoagulants and their mechanism of action
- Hypercoagulability (Definition / Types / Causes / Laboratory testing).

Doctors' notes

Extra

Important

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Resources: 435 Boys' & Girls' slides | Guyton and Hall 12th & 13th edition

Editing file

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Hemostasis: Prevention or **stoppage** of blood loss.

Hemostatic Mechanism

- 1.Vessel wall
- 2.Platelets
- 3.Blood coagulation
- 4.Fibrinolysis

Hemostatic Mechanism

1) Vessel wall

Immediately After injury there is localized **Vasoconstriction.**

Causative Factors	Importance
○ Nervous reflexes ○ Local myogenic spasm ○ Local humoral factors → Thromboxane [TXA2] (Vasoconstrictor)	○ Crushing injuries → Intense spasm → No lethal loss of blood

2) Platelets

Production and activation, Formation of platelet plug **(Primary hemostasis)**

Normal endothelium will secrete	Importance
Normal endothelium will secrete : ○ Nitric oxide [NO] ○ Prostacyclin [PGI1] ○ ADP Phosphatase	○ stop bleeding from small vascular damage

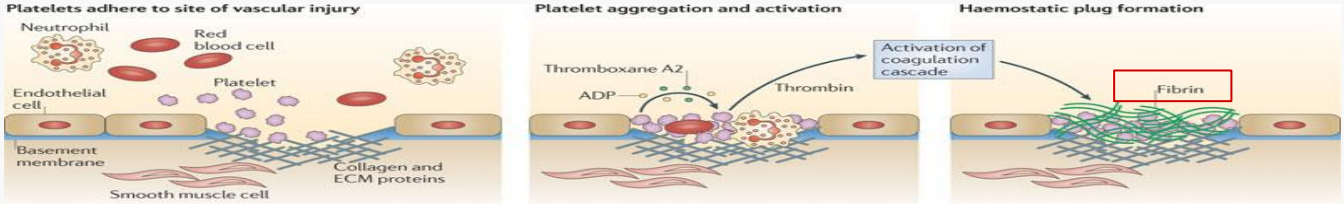
3) Blood coagulation

Formation of **fibrin meshwork** (Threads) to form a **CLOT.(secondary hemostasis)**
(**Blood Clot:** Is composed of a meshwork of fibrin fibers running in all directions and entrapping blood cells, platelets, plasma) Appear red in color whereas the platelet clot appear white

- **Blood clotting** is the transformation of blood (soluble fibrinogen) from a liquid into a solid gel form (insoluble fibrin strands)
- **Pathways :**
  - Intrinsic & Extrinsic [more details in the next slides]

4) Fibrinolysis

normal breakdown of clots



Coagulation reinforces the **platelet plug** with fibrin threads that act as a "molecular glue"

Clotting Factors: Clotting factors mnemonic

Names	Factors
Fibrinogen	**I**
Prothrombin	**II**
Thromboplastin (tissue factor)	**III**
Calcium	**IV**
Labile factor	**V**
Stable factor	**VII**
Antihemophilic factor It's absence lead to hemophilia	**VIII**
Antihemophilic factor B	**IX**
Stuart-prower factor	**X**
Plasma thromboplastin antecedent (PTA)	**XI**
Hageman factor (contact factor)*	**XII**
Fibrin stabilizing factor	**XIII**

- Most of clotting factors are plasma protein and formed in the liver so any problem in liver may lead to either bleeding or thrombosis.
- There is no factor 6 !
- *(Factor 12) is called as " Contact Factor " because it contacts with collagen or subendothelial tissue and become Active.

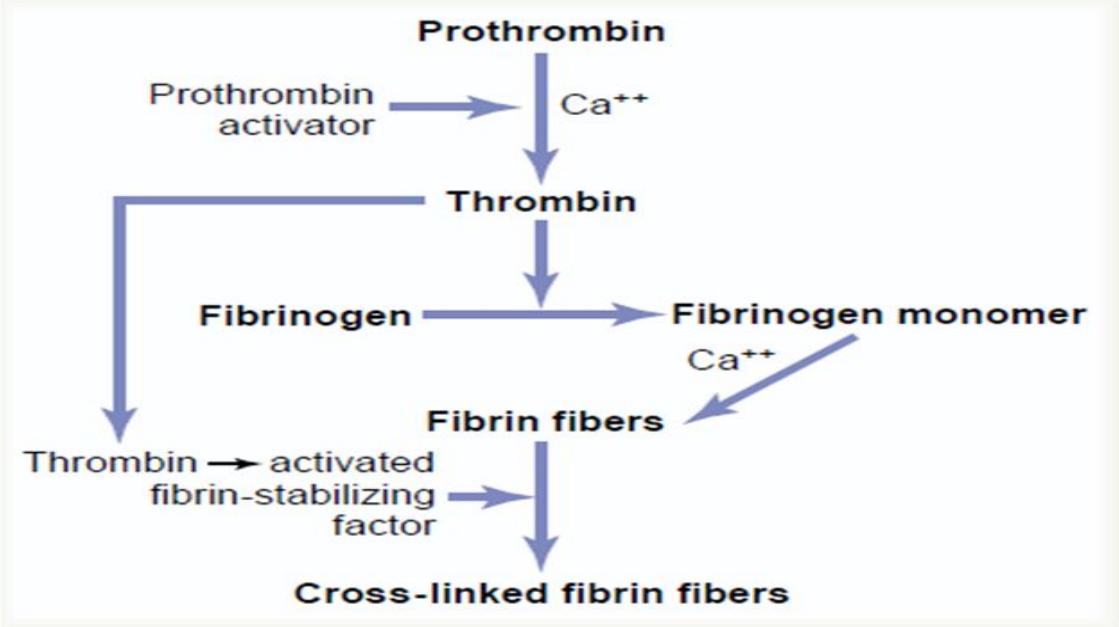
Fibrinogen (factor I):	- Is a high-molecular-weight plasma protein - it is continually formed by the liver. - little or no fibrinogen leak from blood vessels.
Prothrombin (factor II):	- Present in normal plasma in a concentration of 15 mg/dl. - a plasma protein , a2 globulin - It is unstable protein that can be split easily into thrombin. - It is continually formed by the liver. - Vitamin K is important for normal production of prothrombin by the liver. - Lack of vit K or liver disease can decrease the of prothrombin formation to a very low level → bleeding.
Fibrin-stabilizing factor (XIII):	- Is a plasma protein. - It is also released from platelets that is entrapped in the clot. - It must be activated before it affects the fibrin fibers. - Activated XIII factor operates as an enzyme causing additional strength of fibrin meshwork.

Thrombin :

Thrombin: important

- Is a protein enzyme with weak proteolytic capabilities.
- It acts on **fibrinogen** to form one molecule of **fibrin monomer**.
- Fibrinogen is a plasma protein formed in liver
  (Thrombin changes fibrinogen to fibrin)
- Fibrin monomers polymerize with one another to form **fibrin fibers.**
- Thrombin is essential in platelet morphological changes to form **primary plug**
- Thrombin stimulates platelets to release **ADP & thromboxane A2**; both stimulate further platelets aggregation
- Activates factor **V** and factor 8.
- It also activate itself by (positive feed back mechanism).
- The main enzyme of coagulation is the thrombin.
- It activates factor **XIII** (Fibrin stabilizing factor)
- Fibrin is soluble need to be stabilized by the action of factor XIII (13)

Action of thrombin on fibrinogen to form fibrin:



- **GUYTON : Action of Thrombin on Fibrinogen to Form Fibrin.**

Fibrinogen is formed in the liver, and liver disease can decrease the concentration of circulating fibrinogen, as it does the concentration of prothrombin, pointed out earlier. Because of its large molecular size, little fibrinogen normally leaks from the blood vessels into the interstitial fluids, and because fibrinogen is one of the essential factors in the coagulation process, interstitial fluids ordinarily do not coagulate. Yet, when the permeability of the capillaries becomes pathologically increased, fibrinogen does then leak into the tissue fluids in sufficient quantities to allow clotting of these fluids in much the same way that plasma and whole blood can clot.**Thrombin** is a protein *enzyme* with weak proteolytic capabilities. It acts on fibrinogen to remove four low-molecular-weight peptides from each molecule of fibrinogen, forming one molecule of *fibrin monomer* that has the automatic capability to polymerize with other fibrin monomer molecules to form fibrin fibers. Therefore, many fibrin monomer molecules polymerize within seconds into *long fibrin fibers* that constitute the *reticulum* of the blood clot. In the early stages of polymerization, the fibrin monomer molecules are held together by weak noncovalent hydrogen bonding, and the newly forming fibers are not cross-linked with one another; therefore, the resultant clot is weak and can be broken apart with ease. But another process occurs during the next few minutes that greatly strengthens the fibrin reticulum. This involves a substance called *fibrin-stabilizing factor* that is present in normal plasma but is also released from **platelet**s entrapped in the clot. It must be activated. The same thrombin that causes fibrin formation also activates the fibrin-stabilizing factor. Then this activated substance operates as an enzyme to cause *covalent bonds* between more and more of the fibrin monomer molecules, as well as multiple cross-linkages between adjacent fibrin fibers.

Blood coagulation (Clot formation): in general

- A series of biochemical reactions leading to the **formation of a blood clot** within few seconds after injury.
- The role of **platelets** in clot formation and retraction is that they are **contractile units** that hold the clot together.
- **Prothrombin** (inactive thrombin) is activated by a long intrinsic or short extrinsic pathways
- This reaction leads to the **activation of thrombin** enzyme from inactive form prothrombin
- **Thrombin** will change **fibrinogen** (plasma protein) into **fibrin** (insoluble protein)

Intrinsic and Extrinsic Pathway *

Read it then follow the diagrams in the next slide

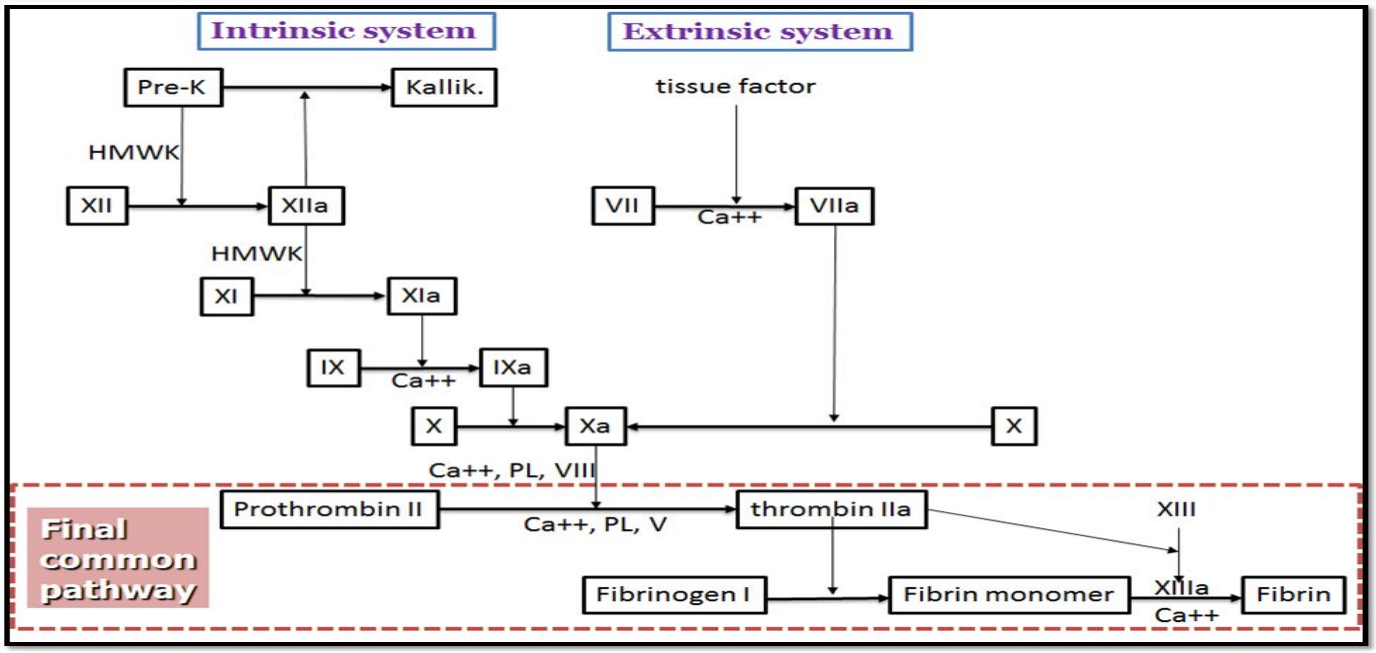
Intrinsic pathway Long pathway	Extrinsic pathway short pathway
• Intrinsic Pathway: all clotting factors present In the blood • The trigger is the activation of factor XII by **contact with foreign surface**, injured blood vessel, and glass. - (Factor 12 = contact factor) - It begins with contact factor normally the blood vessel wall is smooth endothelium any change in smoothness will activate the contact factor → clot formation . • Activated factor XII will activate factor XI • Activated factor XI will activate IX • **Activated factor IX + factor VIII + platelet phospholipid factor (PF3)+ Calcium activate factor X**	• Triggered by material released from damaged tissues **(tissue thromboplastin or Tissue Factor)** • **Tissue thromboplastin + VII + Ca activate X** Factors from outside the blood "extravascular " (eg: tissue thromboplastin)

What is the goal of intrinsic and extrinsic pathway ? formation of fibrin to stabilize the 1ry platelet clot

Following this step (Activation of factor 10) the pathway is common for both intrinsic and extrinsic :

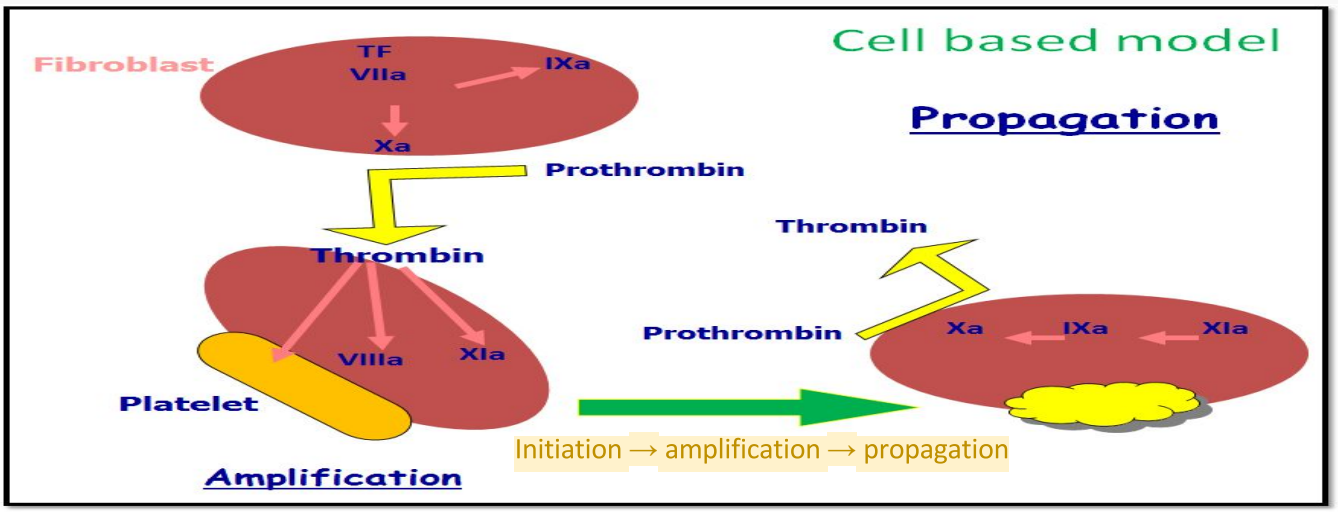
Common pathway

- **Activated factor X + factor V +PF3 + Calcium** activate prothrombin activator; a proteolytic enzyme which activates **prothrombin.**
- Activated prothrombin activates **thrombin**
- Thrombin acts on **fibrinogen** and change it into insoluble thread like **fibrin.**
- **Factor XIII + Calcium > strong fibrin (strong clot)**



Didn't understand? Guyton corner (In the Summary) will help you :)

Cell-based model :



Cell based model means the intrinsic and extrinsic pathways occur on the surface of platelet and endothelium هذا بس اللي مطلوب منكم تعرفونه من هالصورة :)

The role of Calcium in clotting:

- **Calcium plays an important role in coagulation it's needed in many steps.**
- **Blood samples can be <u>prevented from clotting</u> by :**

1. **Citrate ions** → they deionize Calcium
2. **Oxalate ions** → precipitate the Calcium
3. It can also be prevented by other drugs such as **Warfarin** which decreases the production of factors VII, IX and X by the liver.

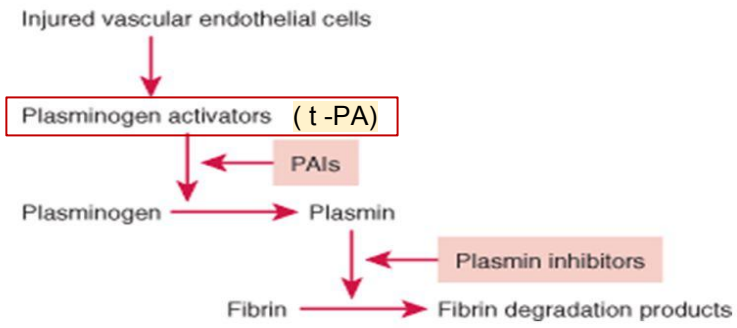
في أكياس الدم يشيلون الكالسيوم عن طريق انهم يضعونهم في أكياس تحتوي على citrate عشان يمنعون تجلط الدم

Fibrinolysis :

- Formed blood clot can either become fibrous or dissolved.
- **Fibrinolysis (dissolving) =** Break down of fibrin by naturally occurring enzyme **PLASMIN** therefore prevent intravascular blocking.
- There is a balance between clotting and fibrinolysis

➔ **Excess clotting:** blocking of Blood Vessels **/ Excess fibrinolysis:** tendency for bleeding.

-Plasmin will break down any fibrin either present in the blood vessel or out of the blood vessel (intravascular and extravascular fibrin) .
-Plasmin breaks down both fibrin and fibrinogen يكسر الفايبرن واللي خلفوه :D
-At the site of injury there will be release of t-PA which activate the plasminogen into its active form plasmin.
- to check if patient has Pulmonary embolism or not .**D-dimer tests** are used to help rule out the presence of an inappropriate blood clot (thrombus).



Fibrin deposition and fibrinolysis must be balanced during repair of an injured blood vessel wall. Injured vascular endothelial cells release plasminogen activators (tissue plasminogen activator, urokinase), activating fibrinolysis. Plasminogen activators cleave plasminogen into plasmin, which dissolves clots. Fibrinolysis is controlled by plasminogen activator inhibitors (PAI-1) and plasmin inhibitors (α2-antiplasmin).

❖ Plasmin :

- Is present in the blood in an inactive form plasminogen
- Is activated by tissue plasminogen activators (t-PA) in blood.
- Digests intra & extra vascular deposit of Fibrin > **(fibrin degradation products (FDP) [D-dimer])**
- **Unwanted** effect of plasmin is the digestion of clotting factors

Plasmin is controlled by:	1. Tissue Plasminogen Activator Inhibitor **(TPAI)** 2. **Antiplasmin** from the liver
Uses:	Tissue Plasminogen Activator (TPA) used to activate plasminogen **to dissolve coronary clots** - t-PA is used in stroke patient we do certain test to determine whether the clot is 3hs formed or before 3hs. - Before 3 hs ⟶ give t-PA ⟶ lysis of fibrin and lysis of clot. - If after 3hs ⟶ we don't give t-PA cuz if we give t-PA it will activate plasmin of normal tissue other than the clot plasmin and break fibrin present in other tissues may lead to bleeding ⟶ death of pt due to hemorrhagic shock.

❖ Enzymatic activation products of coagulation and fibrinolytic mechanisms such as :

1) prothrombin 1+2 (F1+2) **2) Thrombin-antithrombin complex (TAT)**
3) FPA (Fibrinopeptide A) **4) D-dimer**

➔ Are not coded for by specific genes, and their concentrations reflect the overall activation of the coagulation and fibrinolytic systems.

Natural anticoagulants:

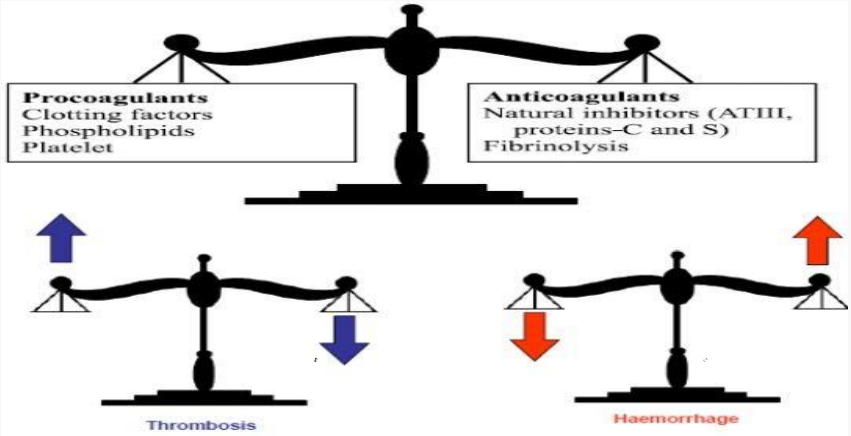
Antithrombin III	• **AT-III Synthesis:** 1) Hepatocytes 2) Endothelial cells. • **Action :** ATIII + thrombin > thrombin-ATIII complex (combines the remaining thrombin and removes it from blood). • **Heparin:** dramatically enhances this action, also it removes factors XII, XI, X, and IX and this can monitored through PTT (partial thrombin time)
Heparin	combines with Antithrombin III and it quickly removes thrombin from blood, Liver, lungs, mast cells, basophils - Heparin naturally occurring in body and can be given as drug (SC-IV)
Endothelial surface factors	1.Smoothness of the Endothelial cells 2.Glycocalyx layer 3.Thrombomodulin protein
Fibrin fibers	adsorbs ~ 90% of thrombin to removes it from circulating blood
Protein C	• **inhibits Va & VIIIa** • **Synthesis:** 1) Hepatocytes 2) Vitamin K-dependent. • **Activated protein C resistance (APC-R):** is mainly due to a genetic abnormality of clotting factor V called (factor V Leiden mutation). point mutation in the factor V gene, G1691A in exon 10, leading to Arg506Gln).
Protein S	• **cofactor for protein C**

Conditions that cause excessive bleeding :

Vitamin K Deficiency	• Prothrombin, Factor VII, Factor IX, Factor X require vitamin K for their synthesis (2,7,9,10) • Hepatitis, Cirrhosis, acute yellow atrophy and GI disease - Warfarin inhibit Vit K dependent factor
Hemophilia	• Increase bleeding tendency. • **X-linked disease.** • Occurs in males only, females are **carriers**. • **85%** due to Factor VIII deficiency (hemophilia A), and **15%** due to Factor IX deficiency (hemophilia B). - B is Milder than A
Thrombocytopenia	• Very low number of platelets in blood (< 50,000/µl) • If less than 10,000 it can be fatal • **Thrombocytopenic purpura** hemorrhages throughout all the body tissues • **Idiopathic Thrombocytopenia** ➔ unknown cause. ➔ Mainly it can be either due to decreased production or increased destruction • **Clinical features:** Easy bruisability, epistaxis, gum bleeding and petechiae

Hemostatic Balance :

- A crucial physiological **balance** exists between factors promoting coagulation (procoagulants) and factors inhibiting coagulation (anticoagulants).
- Coagulation of blood depends on the balance between these two factors.
- Disturbances in this balance could lead to **thrombosis** or **bleeding.**
- The dynamic balance between procoagulant reactions & their down regulation by natural anticoagulants in conjunction with the fibrinolytic system should function within normal parameters **to prevent abnormal thrombus formation or propagation**.
- However, in some instances, alteration of just one variable in this complex series of interacting components will bring about a significant hypercoagulable (prothrombotic) state, which can manifest itself clinically as arterial and/or venous thromboembolism.



U don't have to memorise it it's just an explanation

Virchow Triads 1845 :

❖ **Aetiological factors for thrombosis:**
- Changes in blood flow (stasis) - that's why it's recommended to postoperative pt to walk and not stay in bed
- Changes in the endothelium rough - atherosclerotic vessel susceptible to develop clot formation
- Changes in blood composition (Hypercoagulability) - Hypercoagulability causes : DIC disseminated intravascular coagulation (massive coagulation of circulation all clotting factors are consumed leading to bleeding) ,Infection , pregnancy

Hypercoagulability:

Is a laboratory phenotype whereby activation of the of clotting, fibrinolysis, endothelial cells and platelets are identified.

Hypercoagulability/Prothrombotic States:

Acquired Hemostatic disorders:	• **Raised Levels of fibrinogen & FVII** • Pregnancy and its complications كلما تحمل تسقط لآن الأنتي بوديز عندها كثيرة • Surgery and prolonged immobility orthopedic surgery • Major trauma • Malignancy • Nephrotic syndrome • Dehydration • Hyperviscosity • Polycythaemia • Thrombocytosis • Sepsis • Smoking • Age • Obesity • Varicose veins • Antiphospholipids antibodies(LA,ACAs) eg :SLE • Oestrogen therapy.
Hereditary Hemostatic disorders: RARE	• Factor V Leidin • Prothrombin G20210A • Hyperhomocysteinemia • **Deficiencies of AT III, Proteins C & S** • increased FVIII

Laboratory tests for hypercoagulability: Read it.

Natural anticoagulants:	ATIII,Protein C,Protein S
Fibrinolysis:	PAI-1 ,**FDPs (D-Dimer)** in pulmonary embolism patients.
Coagulation activation markers:	Thrombin-Antithrombin complexes (TAT), Prothrombin fraction 1+2 ,D-Dimer
Activated protein C Resistance (APCR):	Functional Assay ,Genetic assay (Factor V Leiden)
Genotyping:	Factor V Leiden,Prothrombin G20210A, Hyperhomocysteinemia (MTHFR)

SUMMARY

❖ Hemostatic Mechanism :

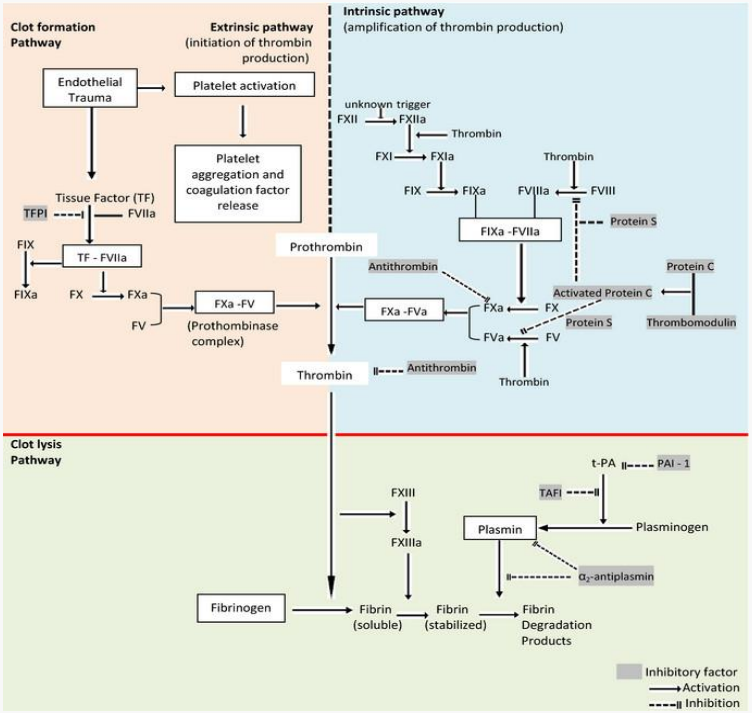
1.Vessel wall : vasoconstriction
2.Platelets : Production and activation, platelets plug formation
3.Blood coagulation : Clot formation (intrinsic & extrinsic pathways)
4.Fibrinolysis : Break down of fibrin by naturally occurring enzyme **PLASMIN** .

❖ Clotting factors :

TABLE 31–5 System for naming blood-clotting factors.

Factor[a]	Names
I	Fibrinogen
II	Prothrombin
III	Thromboplastin
IV	Calcium
V	Proaccelerin, labile factor, accelerator globulin
VII	Proconvertin, SPCA, stable factor
VIII	Antihemophilic factor (AHF), antihemophilic factor A, antihemophilic globulin (AHG)
IX	Plasma thromboplastic component (PTC), Christmas factor, antihemophilic factor B
X	Stuart–Prower factor
XI	Plasma thromboplastin antecedent (PTA), antihemophilic factor C
XII	Hageman factor, glass factor
XIII	Fibrin-stabilizing factor, Laki–Lorand factor
HMW-K	High-molecular-weight kininogen, Fitzgerald factor
Pre-Ka	Prekallikrein, Fletcher factor
Ka	Kallikrein
PL	Platelet phospholipid

[a]Factor VI is not a separate entity and has been dropped.



Fibrinogen (factor I):	- Is a high-molecular-weight plasma protein. - it is continually formed by the liver. - little or no fibrinogen leak from blood vessels.
Prothrombin (factor II):	- Present in normal plasma in a concentration of 15 mg/dl. - a plasma protein , a2 globulin - It is unstable protein that can be split easily into thrombin. - It is continually formed by the liver. - Vitamin K is important for normal production of prothrombin by the liver. - Lack of vit K or liver disease can decrease the of prothrombin formation to a very low level ⟶ bleeding.
Fibrin-stabilizing factor (XIII):	- Is a plasma protein. - It is also released from platelets that is entrapped in the clot. - It must be activated before it affects the fibrin fibers. - Activated XIII factor operates as an enzyme causing additional strength of fibrin meshwork.
Thrombin	-Is a protein enzyme with weak proteolytic capabilities. -It acts on **fibrinogen** to form one molecule of **fibrin monomer**. (Thrombin changes fibrinogen to fibrin) -Fibrin monomers polymerize with one another to form **fibrin fibers.** -Thrombin stimulates platelets to release **ADP & thromboxane A2**; both stimulate further platelets aggregation -Activates factor **V** and factor 8. -It activates factor **XIII** (Fibrin stabilizing factor)

SUMMARY

Mechanism of Blood Coagulation (GUYTON)

Extrinsic Pathway for Initiating Clotting

The extrinsic pathway for initiating the formation of prothrombin activator begins with a traumatized vascular wall or traumatized extravascular tissues that come in contact with the blood. This leads to the following steps, as shown in Figure 36-3:

1. *Release of tissue factor*. Traumatized tissue releases a complex of several factors called *tissue factor* or *tissue thromboplastin*. This factor is composed especially of *phospholipids* from the membranes of the tissue plus a *lipoprotein complex* that functions mainly as a *proteolytic enzyme*.
2. *Activation of Factor X—role of Factor VII and tissue factor*. The lipoprotein complex of tissue factor further complexes with blood coagulation Factor VII and, in the presence of calcium ions, acts enzymatically on Factor X to form *activated Factor X* (Xa).
3. *Effect of Xa to form prothrombin activator—role of Factor V*. The activated Factor X combines immediately with tissue phospholipids that are part of tissue factors or with additional phospholipids released from **platelet**s, as well as with Factor V to form the complex called *prothrombin activator*. Within a few seconds, in the presence of calcium ions (Ca^{++}), this splits prothrombin to form thrombin, and the clotting process proceeds as already explained. At first, the Factor V in the prothrombin activator complex is inactive, but once clotting begins and thrombin begins to form, the proteolytic action of thrombin activates Factor V. This then becomes an additional strong accelerator of prothrombin activation. Thus, in the final prothrombin activator complex, activated Factor X is the actual protease that causes splitting of prothrombin to form thrombin; activated Factor V greatly accelerates this protease activity, and **platelet** phospholipids act as a vehicle that further accelerates the process. Note especially the *positive feedback* effect of thrombin, acting through Factor V, to accelerate the entire process once it begins.

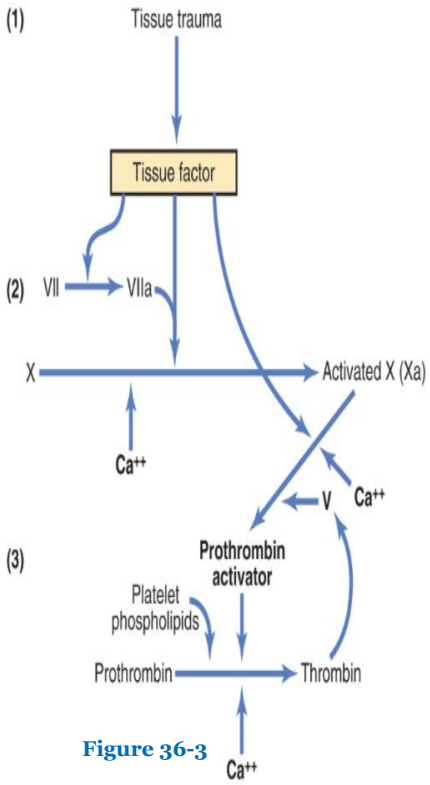


Figure 36-3

Intrinsic Pathway for Initiating Clotting

The second mechanism for initiating formation of prothrombin activator, and therefore for initiating clotting, *begins with trauma to the blood or exposure of the blood to collagen* from a traumatized blood vessel wall. Then the process continues through the series of cascading reactions shown in Figure 36-4

1. *Blood trauma causes (1) activation of Factor XII and (2) release of **platelet** phospholipids.*Trauma to the blood or exposure of the blood to vascular wall collagen alters two important clotting factors in the blood: Factor XII and the **platelet**s. When Factor XII is disturbed, such as by coming into contact with collagen or with a wettable surface such as glass, it takes on a new molecular configuration that converts it into a proteolytic enzyme called "activated Factor XII." Simultaneously, the blood trauma also damages the **platelet**s because of adherence to either collagen or a wettable surface (or by damage in other ways), and this releases **platelet** phospholipids that contain the lipoprotein called ***platelet**factor 3,* which also plays a role in subsequent clotting reactions.
2. *Activation of Factor XI*. The activated Factor XII acts enzymatically on Factor XI to activate this factor as well, which is the second step in the intrinsic pathway. This reaction also requires *HMW (high-molecular-weight) kininogen* and is accelerated by prekallikrein.
3. *Activation of Factor IX by activated Factor XI*. The activated Factor XI then acts enzymatically on Factor IX to activate this factor as well.
4. *Activation of Factor X—role of Factor VIII*. The activated Factor IX, acting in concert with activated Factor VIII and with the **platelet** phospholipids and factor 3 from the traumatized **platelet**s, activates Factor X. It is clear that when either Factor VIII or **platelet**s are in short supply, this step is deficient. Factor VIII is the factor that is missing in a person who has classic *hemophilia,* for which reason it is called *antihemophilic factor*.**Platelet**s are the clotting factor that is lacking in the bleeding disease called *thrombocytopenia*.
5. *Action of activated Factor X to form prothrombin activator—role of Factor V*. This step in the intrinsic pathway is the same as the last step in the extrinsic pathway. That is, activated Factor X combines with Factor V and **platelet** or tissue phospholipids to form the complex called *prothrombin activator*. The prothrombin activator in turn initiates within seconds the cleavage of prothrombin to form thrombin, thereby setting into motion the final clotting process

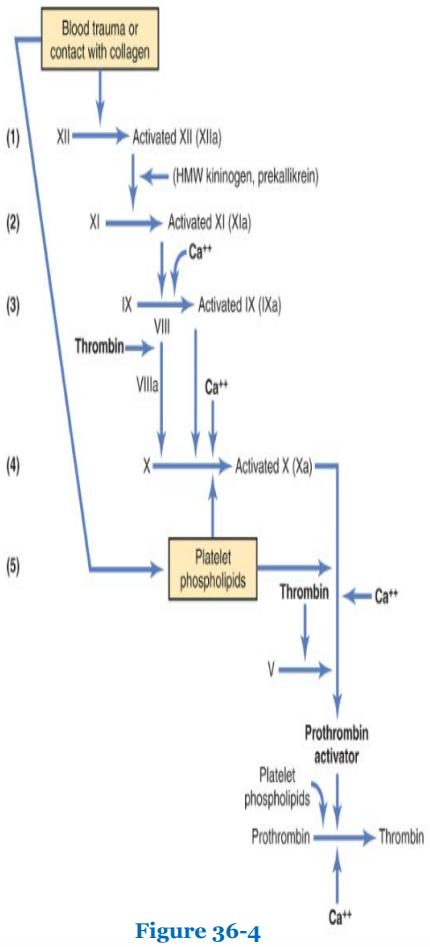
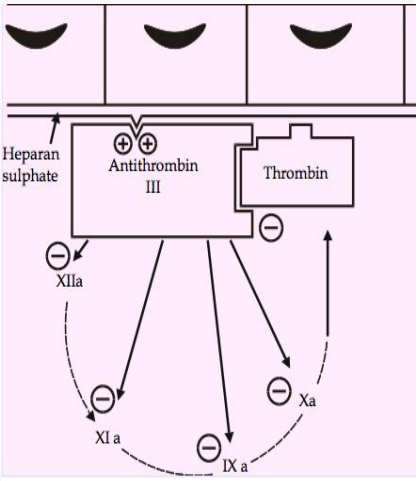


Figure 36-4

SUMMARY

❖ Natural anticoagulants:



- **Antithrombin III :** combines the remaining thrombin and removes it from blood
- **Protein C :** Protein C is a major plasma anticoagulant that acts at the surface of endothelial cells. Activated Protein C neutralizes Factors Va and VIIIa, which effectively blocks the amplification and propagation of coagulation. Protein C is a vitamin K-dependent protein, synthesized in the live.
- **Protein S :** cofactor for protein C
- **Heparin :** combines with Antithrombin III and it quickly removes thrombin from blood.

❖ Abnormal conditions that cause bleeding tendency :

Vitamin K Deficiency	• Prothrombin, Factor VII, Factor IX, Factor X require vitamin K for their synthesis • Hepatitis, Cirrhosis, acute yellow atrophy and GI disease
Hemophilia	• Increase bleeding tendency. • **X-linked disease.** • Occurs in males only, females are **carriers**. • **85%** due to Factor VIII deficiency (hemophilia A), and **15%** due to Factor IX deficiency (hemophilia B).
Thrombocytopenia	• Very low number of platelets in blood (< 50,000/µl) • If less than 10,000 it can be fatal • **Thrombocytopenic purpura** hemorrhages throughout all the body tissues • **Idiopathic Thrombocytopenia** ➔ unknown cause. ➔ Mainly it can be either due to decreased production or increased destruction • **Clinical features:** Easy bruisability, epistaxis, gum bleeding and petechiae

Note : aspirin not anticoagulant its antiplatelet it act on (inhibit) TXA2

MCQs

1- Extrinsic pathway is triggered by : *

A – Factor XII
B – Factor III
C – Factor VIII
D – Factor V

2-Vitamin K is essential for synthesis of Factors:

A- X
B- Ix
C- II & VII
D- All of them

3-Which one of the following stimulates platelets to release TXA2&ADP:

A- Fibrinogen
B- Thrombin
C- fibrin- stabilizing
D- Calcium

4-Blood clot composed of which of the following:

A- Platelets
B- Plasma
C- Blood cells
D- All of them

5-Intrinsic pathway get started by: +

A- Factor VIII
B- tissue factor
C- Hageman factor
D- All of them

6-Which of the following granulocytes most likely contribute in anticoagulation:

A- Neutrophils
B- Basophils
C- Eosinophils
D- monocytes

7-Which of the following true about hemophilia:

A- X-linked disease

B- Depend on vitamin K

C- Affect female mostly

D- Factor V becomes resistant to protein C

8-Heparin enhances action which one of the following:

A- Plasmin

B- Protein c

C- Antithrombin III

D- Tissue plasminogen activator

9-factor V Leiden mutation causes hypercoagulation:

A- True
B- False

10-Hemophilia A is caused by deficiency of

A- Factor V
B- Factor iX
C- Factor Viii
D- B & C

* Tissue thromboplastin or Tissue Factor) = Factor III

+ Hageman factor = contact factor = factor XII

answer key: 1:B , 2:D , 3:B , 4:D , 5:C , 6:B , 7:A , 8:C , 9:A , 10:C.

خولة العمَّاري
نجود الحيدري
نورة الطويل
لولوة الصغير
لجين السواط
رزان السبتي
ربى السليمي
ديما الفارس
خولة العريني
ملاك الشريف
منيرة الحسيني
مروج الحربي
أفنان المالكي
دلال الحزيمي
رناد القحطاني
سارة الخليفة
فرح مندوزا
مي العقيل
نورة الخراز
سارة الخليفة
نورة الخيال
رغد النفيسة
منيرة السلولي
نوف العبدالكريم
سها العنزي
نورة القحطاني

عمر آل سليمان
عبدالعزيز الحماد
عبدالرحمن السياري
محمد أبونيان
عبدالرحمن البركه
إبراهيم النفيسه
محمد البشر
عمر العتيبي
حمزة الفعر
عبدالله الجعفر
عبدالله الضحيان
حسن البلادي
حسن الشماسي
محمد الفواز
محمد السحيباني
وائل العود
رواف الرواف
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