Physiology Team

LECTURE 3

Coagulation Mechanisms

HAEMATOLOGY BLOCK

DONE BY:
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REVISED BY:
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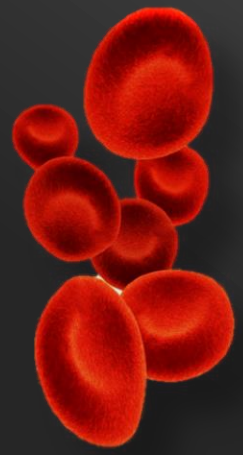

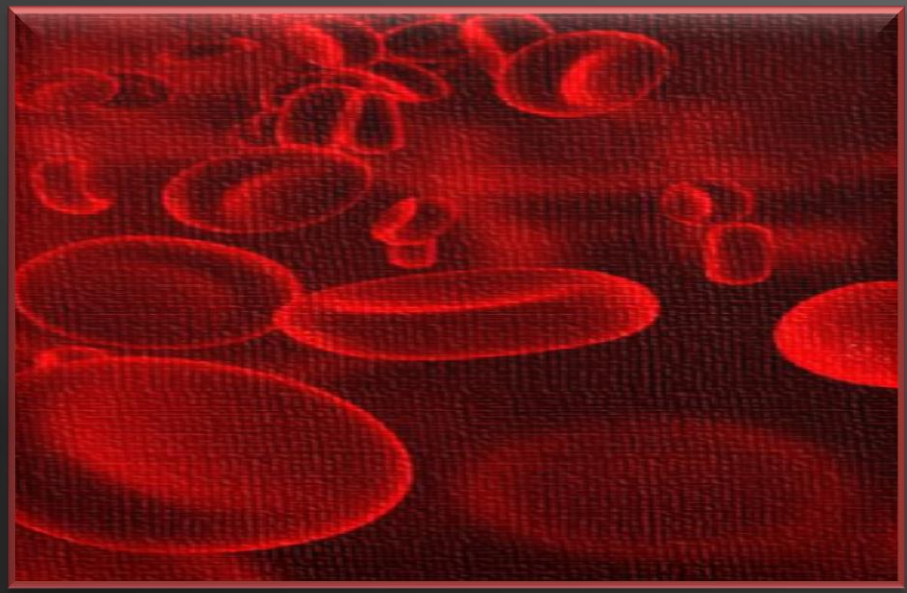

OBJECTIVES

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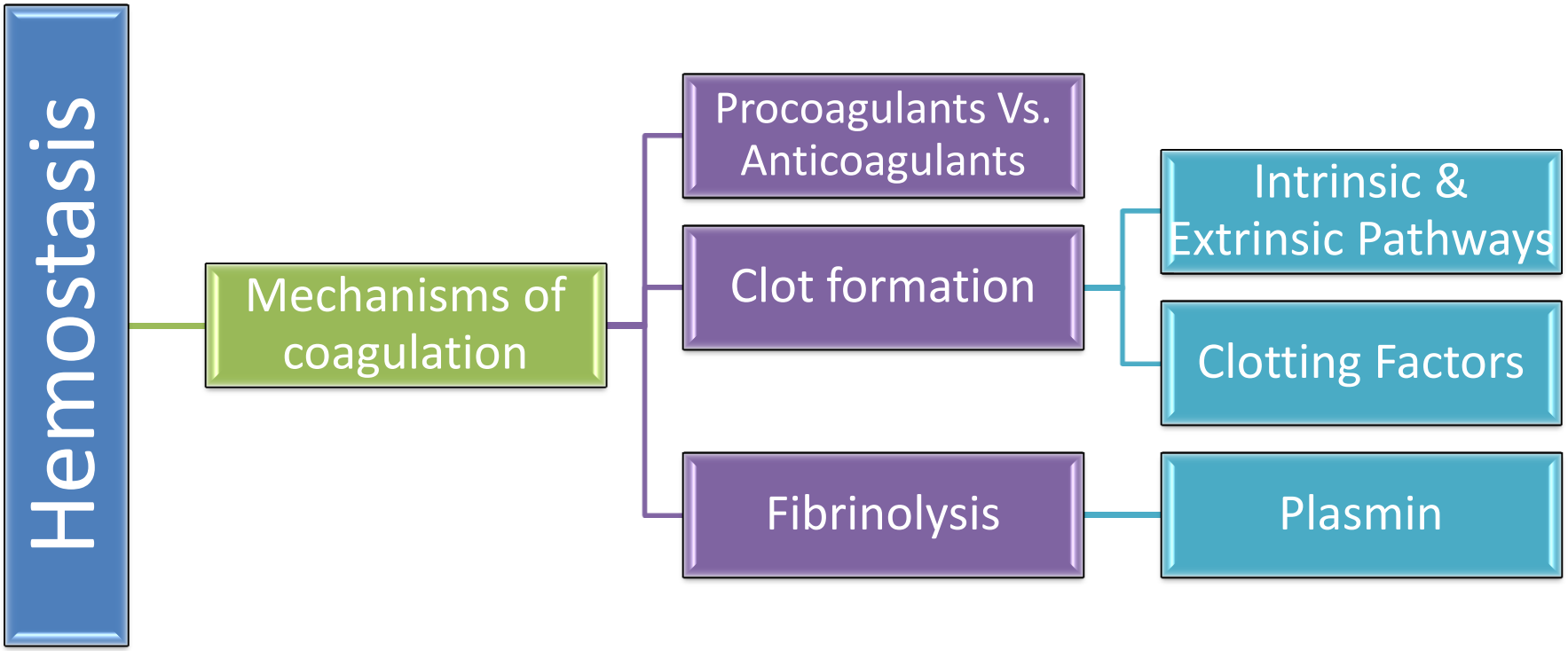
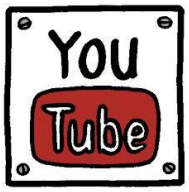
At the end of this lecture, student should be able to:

- 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



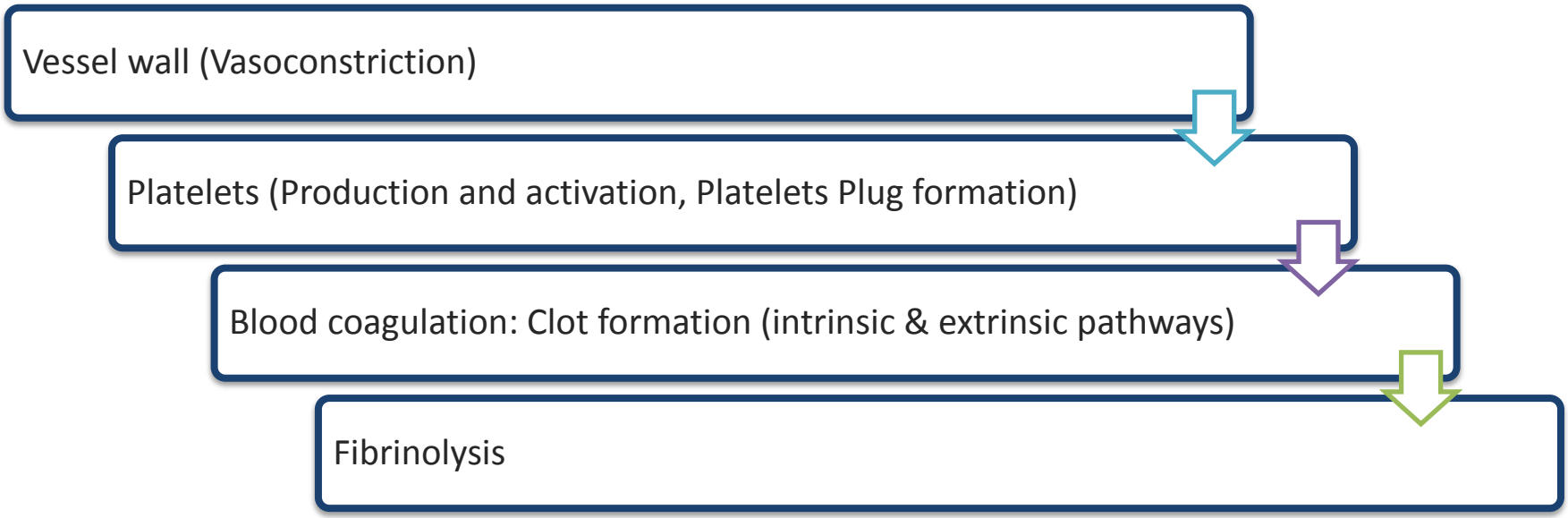


Great video to help you understand:

Just click on the previous You Tube icon (:

Hemostasis is the prevention or stoppage of blood loss.

Hemostatic Mechanisms:



Coagulation: Formation of fibrin meshwork (Threads) to form a *CLOT*!

*** The fibrin is like الاسمنت that holds the platelets together :D**

Mechanism of Blood Coagulation

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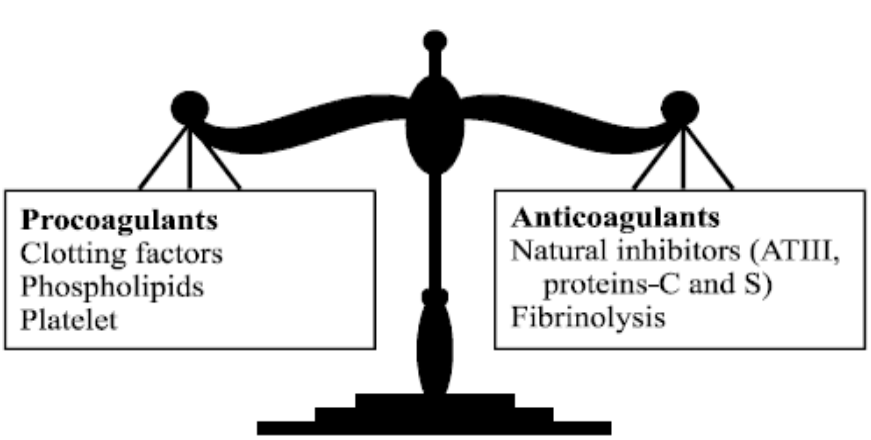
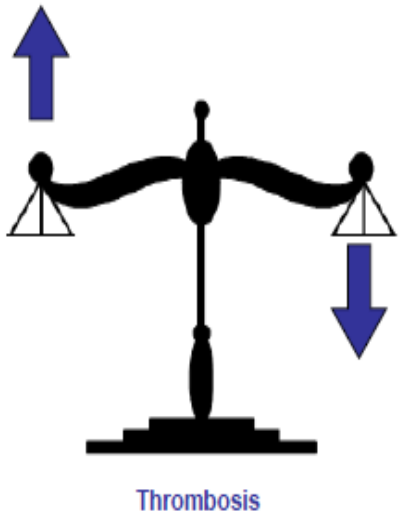
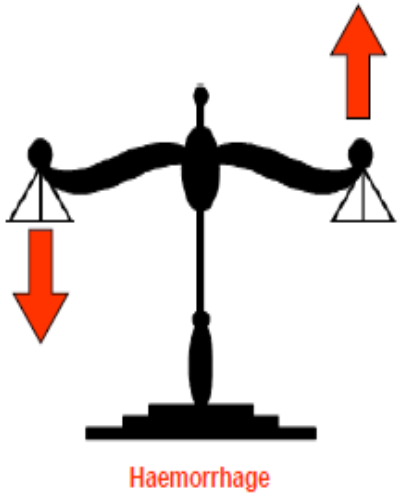
- A crucial physiological *balance* exists between factors promoting coagulation (**procoagulants**) and factors inhibiting coagulation (**anticoagulants**).
- Coagulation of blood depends on the balance between these two factors.
- **Disturbances** in this balance could lead to thrombosis or bleeding and those two are the most common problems in all hospitals!







Clotting Factors

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

They will never ask about the number of the factor or vice versa :)

*They all circulate in the inactive form!

Prothrombin (factor II)

- is a plasma *protein*, α2-globulin.
- present in normal plasma in a concentration of 15 mg/dl.
- it is **unstable** protein that can be split easily into **thrombin**.
- it is continually formed by the *liver*. Vit K dependent.

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.

*The liver depends on vit K in the production of factor 2,7,9 and 10!

Thrombin

- is a protein enzyme with proteolytic capabilities.
- it acts on fibrinogen to form one molecule of fibrin monomer.
- fibrin monomers polymerize with one another to form fibrin fibers.
- it activates **factor XIII**.

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. هو الاسمنت للفايبرن!

Fibrinogen (factor I)

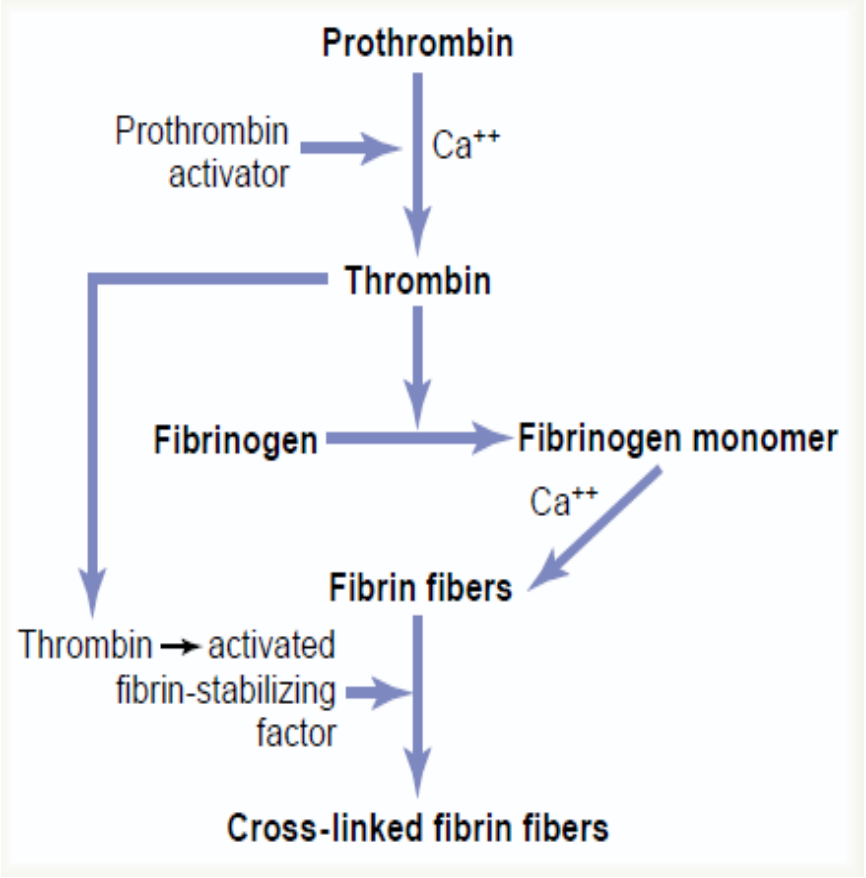
- is a high-molecular-weight plasma protein.
- it is continually formed **by the liver**.
- little or no fibrinogen leak from blood vessels .Because it has high molecular weight it doesn't go out from the circulation!

*Blood Clot "Red Clot":

Is composed of a meshwork of fibrin fibers running in all directions and entrapping **blood cells**, **platelets**, **plasma**.

Thrombin

- Thrombin changes fibrinogen to fibrin.
- Thrombin is essential in platelet **morphological changes** to form primary plug. Change platelet's shape.
- Thrombin stimulates platelets to release ADP & thromboxane A2; both stimulate further platelets aggregation.
- Activates factor V, VIII and XIII.



Blood coagulation (clot formation)

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- A series of biochemical reactions leading to the formation of a blood clot within few seconds after injury.
- 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 Pathway:

- The trigger is the activation of factor XII by contact with foreign surface, injured blood vessel, and glass.
- Activated factor XII will activate factor XI
- Activated factor Xl will activate IX
- Activated factor IX + factor VIII + platelet phospholipid factor (PF3)+ Ca activate factor X.

Extrinsic Pathway:

- Triggered by material released from damaged tissues (tissue thromboplastin)
- Tissue thromboplastin + VII + Ca >> activate X

Common pathway for both intrinsic and extrinsic pathways:

- Activated factor X + factor V +PF3 + Ca 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)

Cont... Pathways

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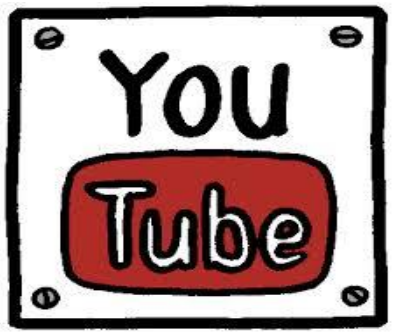
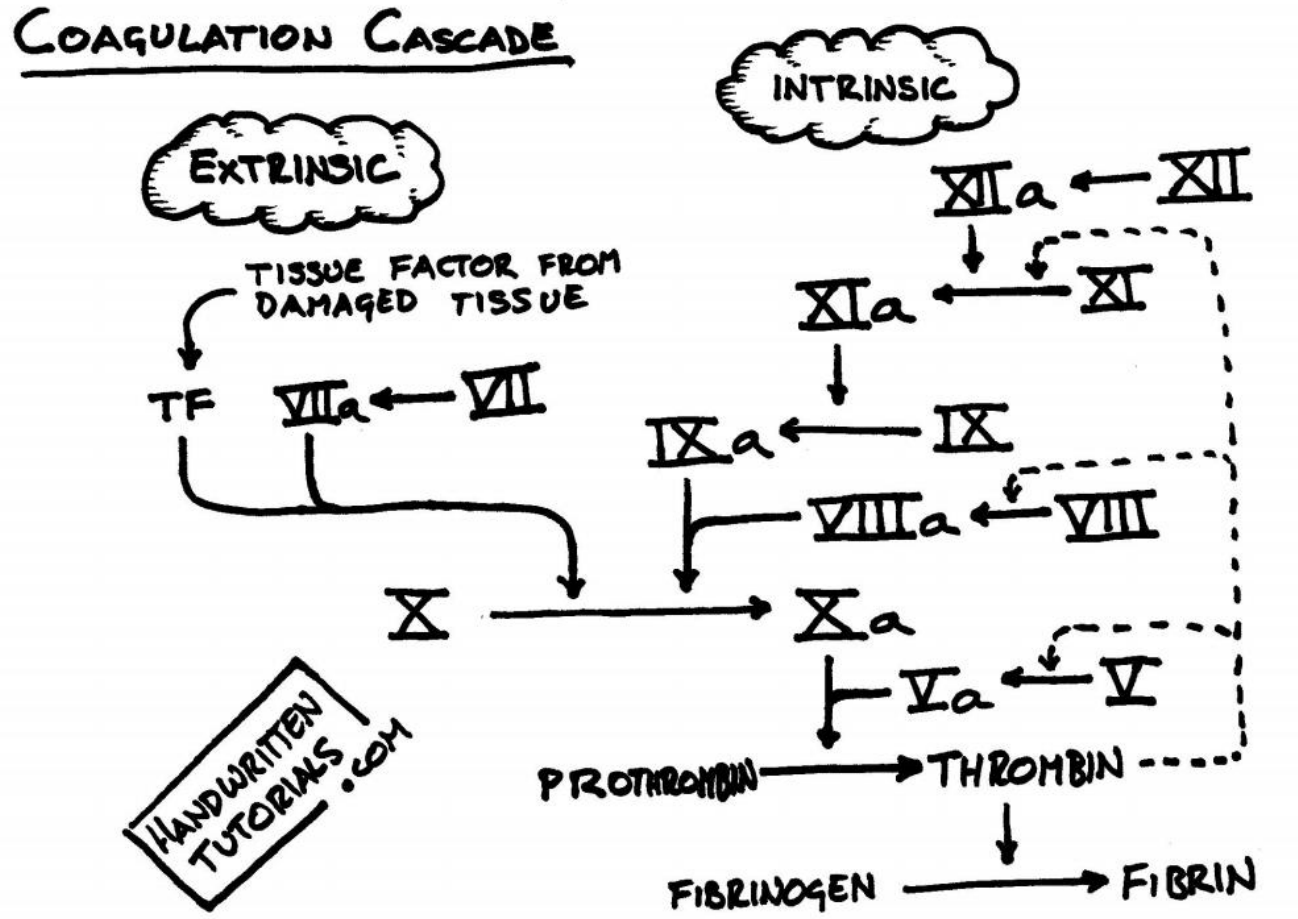


Check out this video it will make it easier for you :D!

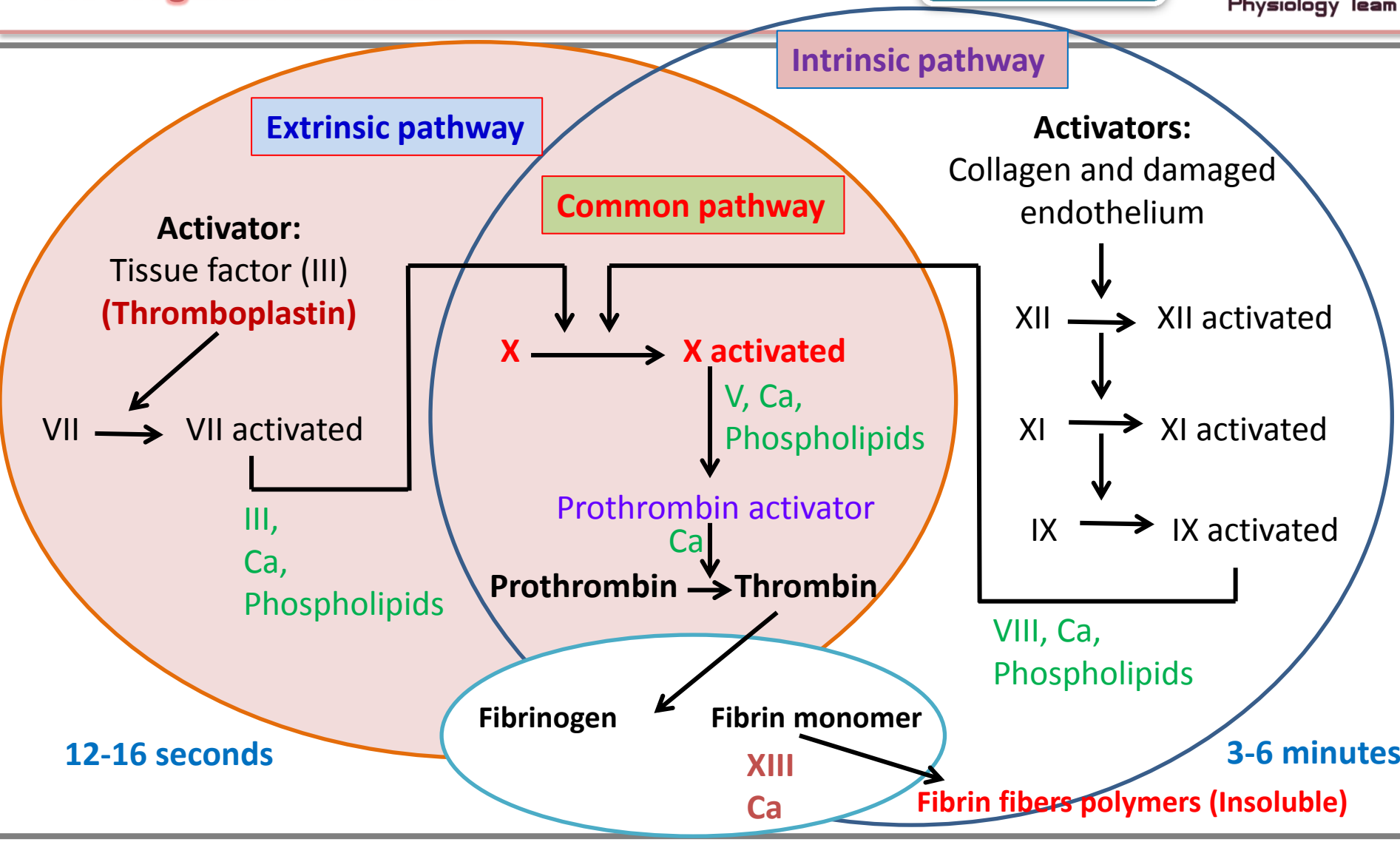
Click on the YouTube icon please

Thanks for Shaikha AlDossary

☺



The Coagulation Cascades



Fibrinolysis

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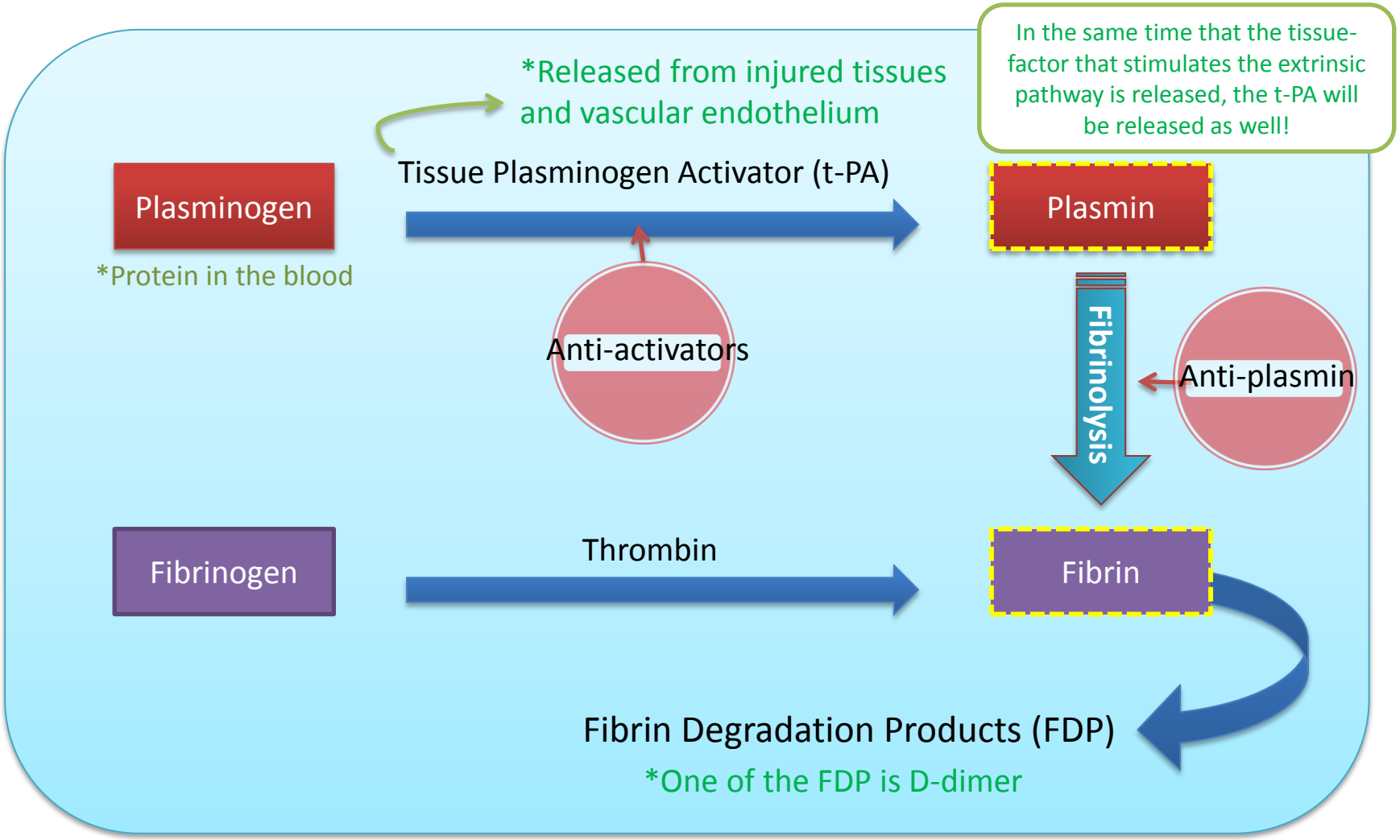
- It's the normal healing!
- Formed blood clot can either become fibrous or dissolved.
- Fibrinolysis (dissolving) = *Break down* of fibrin by naturally occurring enzyme **plasmin** therefore **prevent intravascular blocking**.

- There is a balance between clotting and fibrinolysis:
  - Excess clotting → blocking of Blood Vessels.
  - Excess fibrinolysis → tendency for bleeding.

Fibrinolysis



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).
- Unwanted effect of plasmin is **the digestion of clotting factors**.

- **Plasmin is controlled by:**
  - Tissue Plasminogen Activator Inhibitor (TPAI) "Anti-activators".
  - Antiplasmin from the liver.

- **Uses:**
  - Tissue Plasminogen Activator (TPA) used to activate plasminogen to dissolve coronary clots

Prevention of blood clotting

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Prevention of blood clotting in the **normal** vascular system and *Anticoagulants*:

- Endothelial surface factors:
  - **Smoothness** of the ECS.
  - Glycocalyx layer.
  - Thrombomodulin protein.

- **Fibrin fibers,** adsorbs ~ 90% of thrombin to removes it from circulating blood.

- **Antithrombin III,** combines the remaining thrombin and removes it from blood.

- **Heparin,** combines with Antithrombin III and quickly removes thrombin from blood.

  Heparin can be synthesized in: Liver, lungs, mast cells, basophils.

Anticoagulants for clinical use:

- **Heparin:**
  - commercial, extracted from animals
- **Coumarins:**
  - warfarin, competitive with Vit. K
  - Decrease Factors II, VII, IX, X

Prevention of blood coagulation outside the body:

(decrease calcium ion concentration)

- **Oxalate** (precipitation, toxic)
- **Citrate** (deionizer)
- **EDTA** (Chelating agent)

Conditions that cause excessive bleeding

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- **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**
  - ↑ bleeding tendency.
  - X-linked disease.
  - Affects males.
  - 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).
  - Thrombocytopenia purpura, hemorrhages throughout all the body tissues
  - Idiopathic Thrombocytopenia, unknown cause.

SUMMARY

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- Coagulation is the formation of fibrin meshwork (Threads) to form a clot.
- Coagulation of blood depends on the balance between procoagulants and anticoagulants.
- Prothrombin is the inactive form of thrombin.
- The liver depends on vit K in the production of factor 2,7,9 and 10.
- Thrombin changes fibrinogen to fibrin and it activates factor V, VIII and XIII.
- Blood Clot is composed of a meshwork of **fibrin fibers** running in all directions and entrapping blood cells, platelets, plasma.
- Fibrinolysis is the break down of fibrin by **naturally** occurring enzyme plasmin therefore *prevent intravascular blocking*.
- Plasmin is controlled by: Anti-activators and Antiplasmin.
- **Prevention of blood clotting in the normal vascular system by:** Endothelial surface factors, Fibrin fibers, Antithrombin III and Heparin.
- **Conditions that cause excessive bleeding**: Vitamin K Deficiency, Hemophilia and Thrombocytopenia.

QUESTIONS

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YOU CAN test yourself from here

Click on the question mark

THE END

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If there are any Problems or Suggestions,
Feel free to contact us:

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THANK YOU

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