COAGULATION MECHANISM

Color index

- Important
- Further explanation

Contents

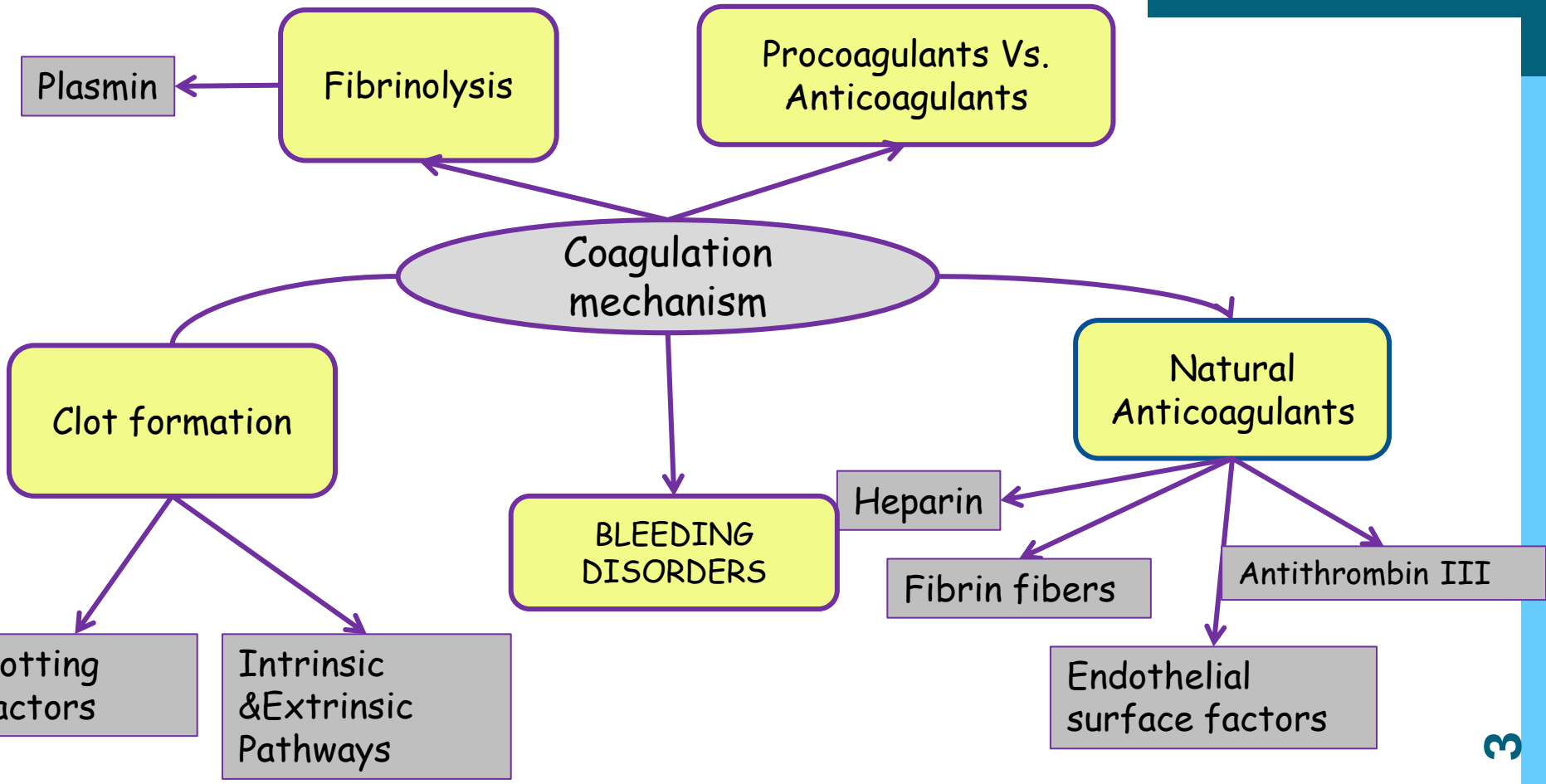
Coagulation Cascade

Blood Coagulation and wound healing

Very helpful

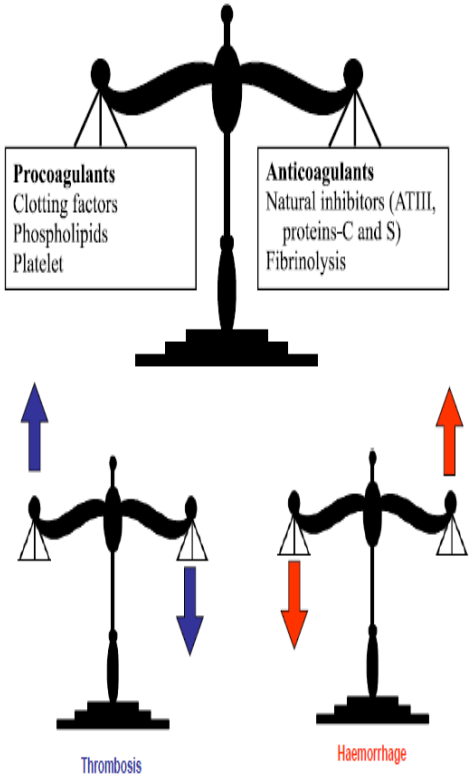
Please check out this link before viewing the file to know if there are any additions/changes or corrections. The same link will be used for all of our work Physiology Edit

Mind map


Plasmin
Fibrinolysis
Procoagulants Vs. Anticoagulants
Coagulation mechanism
Clot formation
BLEEDING DISORDERS
Natural Anticoagulants
Heparin
Fibrin fibers
Antithrombin III
Endothelial surface factors
Clotting Factors
Intrinsic &Extrinsic Pathways

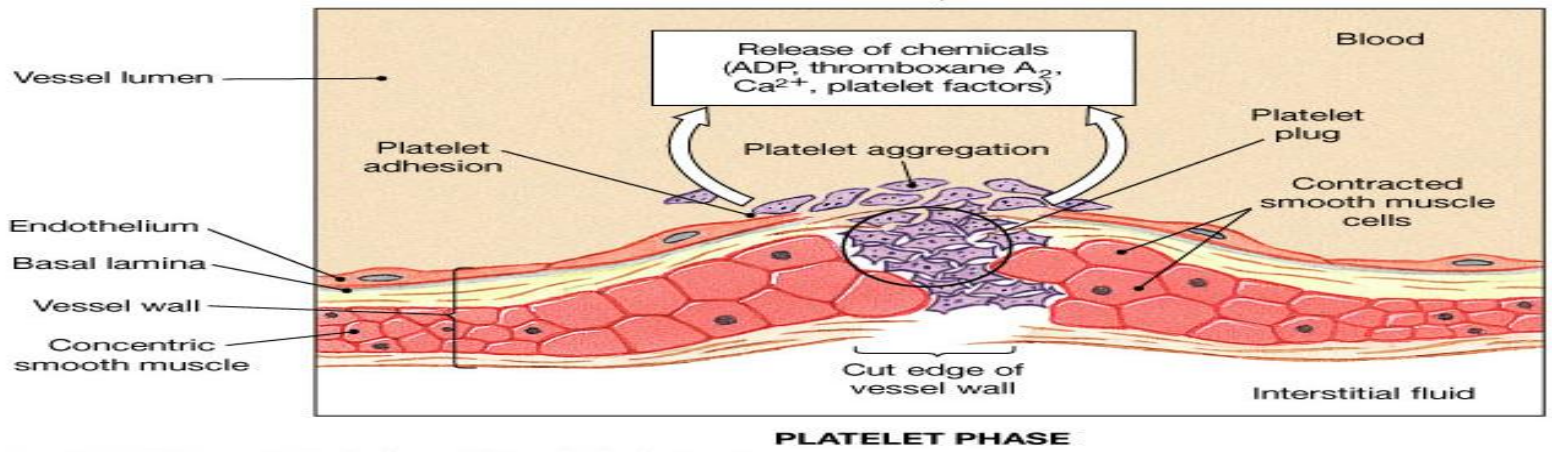
MECHANISM OF BLOOD COAGULATION

- 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:
  - Thrombosis
  - Bleeding



MECHANISM OF BLOOD COAGULATION

- **Hemostasis:** prevention or stoppage of blood loss. (Hemo=blood & stasis=stopping)
- **Hemostatic Mechanisms:**
  - Vessel wall (vasoconstriction) ➡ Platelets (Production and activation, platelets plug formation) ➡ Blood coagulation (Formation of fibrin to form a clot) ➡ Fibrinolysis
- **Coagulation:** is the formation of fibrin meshwork (threads) to form a clot



BLOOD CLOTTING FACTORS

Factor	Name
I	Fibrinogen
II	Prothrombin
III	Thromboplastin (tissue factor)
IV	Calcium
V	Labile factor
VII	Stable factor
VIII	Antihemophilic factor
IX	Christmas factor (Antihemophilic factor B)
X	Stuart-Power factor
XI	Plasma thromboplastin antecedent (PTA)
XII	Hagman factor
XIII	Fibrin stabilizing factors

NB: there's no factor VI

1st letter of each factor

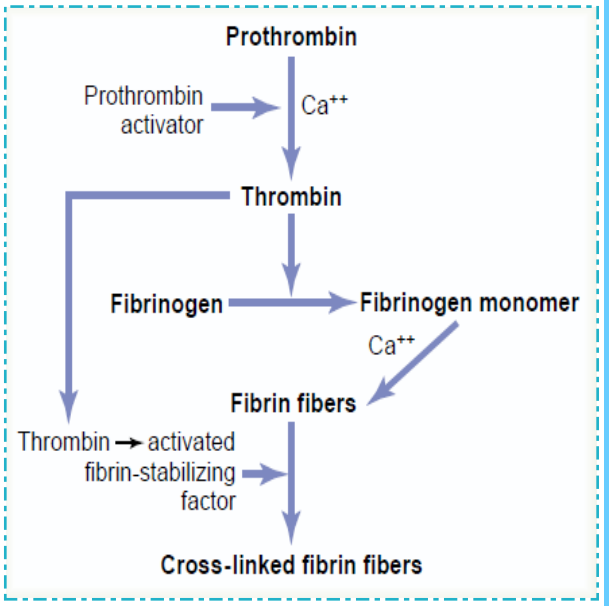
Mnemonic

Foolish People Try Climbing Long Slopes, After Christmas Some People Have Fallen

Prothrombin (factor II):

- 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
- **Vitamin K*** is important for normal production of prothrombin by the liver
- Prothrombin formation decreases in:
  - Liver diseases
  - Lack of vit K leads to bleeding

Vitamin K is essential for synthesis of Factor **II**, **VII**, **IX**, **X**



Thrombin:

- Protein enzyme with weak proteolytic capabilities
- Acts on fibrinogen to form one molecule of fibrin monomer
- Fibrin monomers polymerize with one another to form fibrin fibers
- it activates factor **XIII**, **V**
- Thrombin stimulates platelets to release:
  - ADP
  - thromboxane A2

  ⇒ stimulate further platelets aggregation
- Thrombin is essential in platelet morphological changes to form primary plug

BLOOD CLOTTING FACTORS

Fibrinogen (factor I):

- High-molecular-weight plasma protein
- It is continually formed by the liver
- Little or no fibrinogen leak from blood vessels

Dr.nervana said she doesn't care about the details here, focus more on the factor's ID (name and number)

Fibrin-stabilizing factor (XIII):

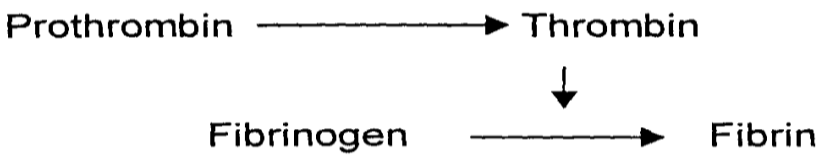
- Plasma protein
- Released from platelets that is entrapped in the clot
- It must be activated before it affects the fibrin fibers
- Activated XIII factor operates as an enzyme causing additional strength of fibrin meshwork

Blood Clot:

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

BLOOD COAGULATION

- 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

Contact with foreign surface, injured blood vessel, and glass

kalik ← Pre k

HMWK* ↓

XII → XIIa

HMWK ↓

XI → XIa

↓

IX → IXa (Ca++)

↓

X → Xa ← X (Ca ,PL ,VIII)

Extrinsic Pathway

Tissue factor (Factor III)

↓

VIIa ← VII (Ca++)

3 + 7 = 10.. Extrinsic pathway is as simple as that!

You were counting down.. 12,11,9- oh you missed 10.. Thus, you got the intrinsic pathway

Common Pathway

Prothrombin II → thrombin IIa (Ca ,PL ,V)

XIII ↓

Fibrinogen I → Fibrin monomer → Fibrin (XIIIa, Ca++)

*HMWK= High molecular weight kininogen *PL= Phospholipid

Things in grey in this slide are not extra, you should know them

COAGULATION CASCADE

*نفس الشريحة السابقة لكن شرح

Intrinsic pathway	Extrinsic pathway	Common pathway
▪ Clotting factors are present in the blood 1. The trigger is the **activation of factor XII** by (foreign surface, injured blood vessel, and glass) 2. Activated factor XII will **activate factor XI** 3. Activated factor Xl will **activate IX** 4. Activated factor IX + factor VIII + platelet phospholipid factor (PF3)+ Ca **activate factor X** 5. Common pathway follows..	▪ fast and short ▪ Triggered by material released from damaged tissues (tissue thromboplastin) ▪ (Tissue thromboplastin + VII + Ca) **activate X** ▪ Common pathway follows..	▪ Activated(factor X + factor V +PF3 + Ca) **activate prothrombin activator;** a proteolytic enzyme which activates prothrombin. ▪ prothrombin **activates thrombin** ▪ Thrombin acts on fibrinogen and change it into insoluble thread like fibrin ▪ Factor XIII + Calcium = strong fibrin

Click HERE for khan's academy's video

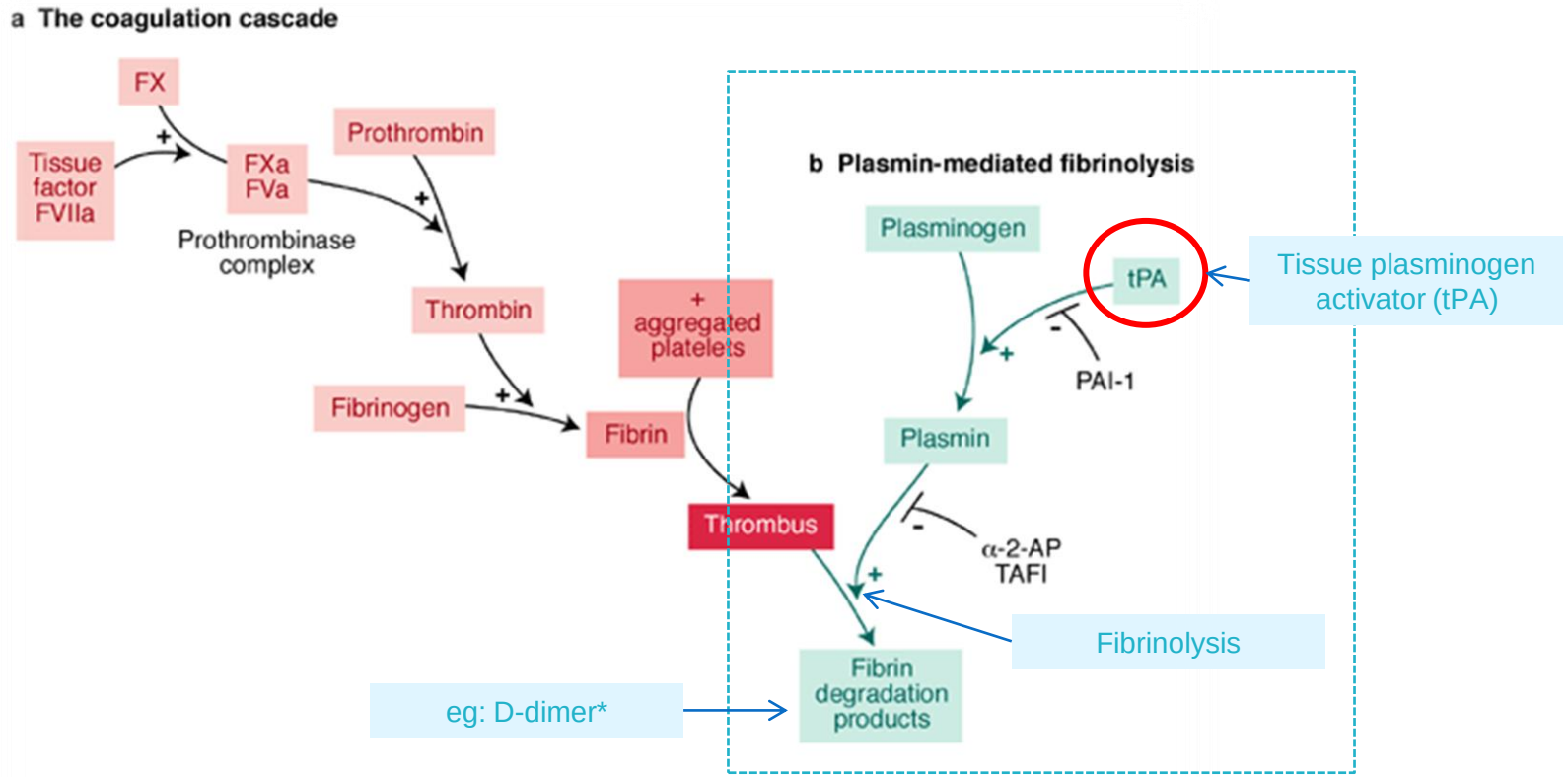
FIBRINOLYSIS

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

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
  - Antiplasmin from liver
- Tissue Plasminogen Activator (TPA) used to activate plasminogen to dissolve coronary clots

FIBRINOLYSIS



Summary of the coagulation and fibrinolysis cascades

*Marker for fibrinolysis

INTRAVASCULAR ANTICOAGULANTS

❑**Endothelial surface factors**
-Smoothness of the endothelial cells (ECs)
-Glycocalyx layer
-Thrombomodulin protein
Thrombomodulin Protein binds to thrombin → Activates Protein C (with Protein S) → inactivates factors V & VIII
Inactivates an inhibitor of tPA → increasing the formation of plasmin
❑ **Fibrin fibers** 90% of thrombin to removes it from circulating blood
❑**Antithrombin III** combines the remaining thrombin and removes it from blood
❑**Heparin** (Increase the effectiveness of Antithrombin III)combines with Antithrombin III and quickly removes thrombin from blood Produced by
- Mast cells
- Basophil cells
❑**Protein C** (inhibits Va & VIIIa) & **Protein S** (Cofactor)

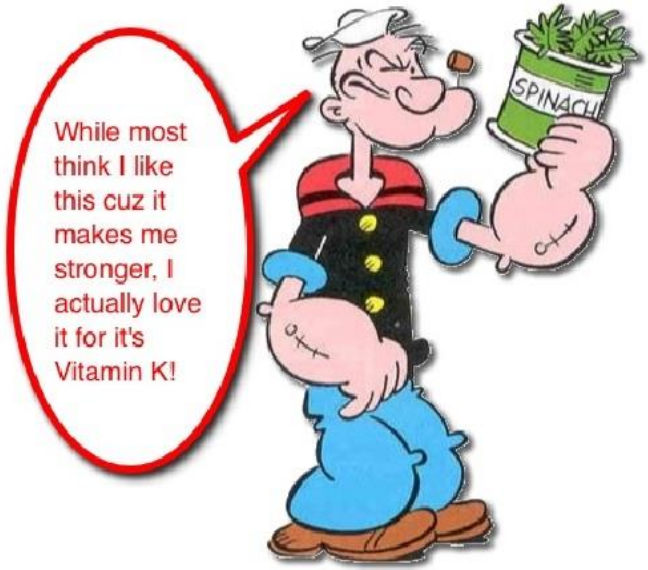
CONDITIONS THAT CAUSE EXCESSIVE BLEEDING

Bleeding

Thrombocytopenia:
Very low number of platelets in blood
Thrombocytopenia purpura, hemorrhages throughout all the body tissues
Idiopathic Thrombocytopenia

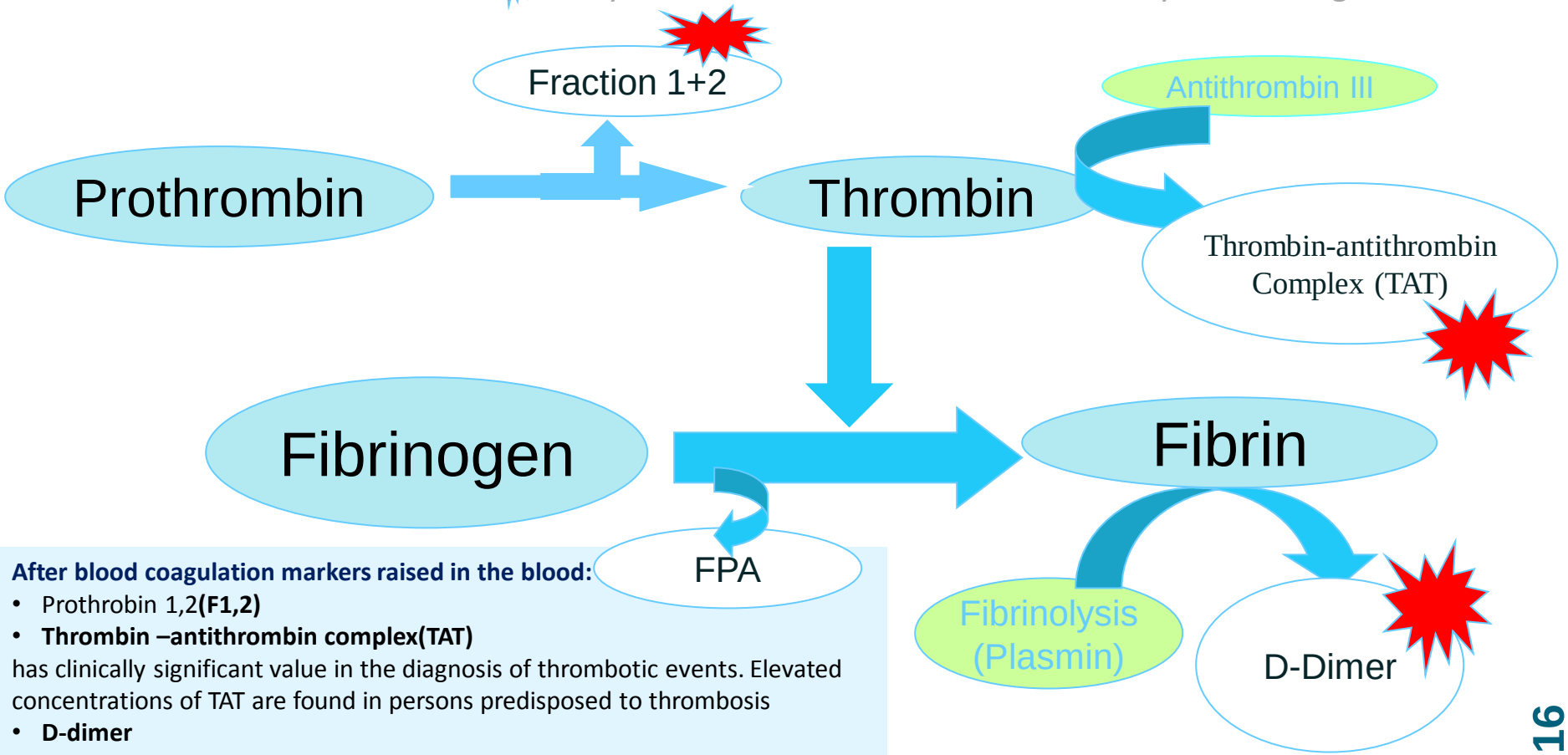
Vitamin K Deficiency:
Hepatitis, Cirrhosis, acute yellow atrophy AND GI disease

Hemophilia
X-linked disease, Affects males.
85% due to Factor VIII deficiency (hemophilia A)
15% due to Factor IX deficiency (hemophilia B).



HEMOSTATIC ACTIVATION MARKERS

memorize names marked in red They are the activation markers of fibrinolysis and coagulation



After blood coagulation markers raised in the blood:

- Prothrobin 1,2**(F1,2)**
- **Thrombin –antithrombin complex(TAT)**

has clinically significant value in the diagnosis of thrombotic events. Elevated concentrations of TAT are found in persons predisposed to thrombosis

- **D-dimer**

(fibrin degradation products)

NATURAL ANTICOAGULANTS

Anti-thrombin III

- Synthesized by hepatocytes and endothelial cells
- Action: ATIII + thrombin → Thrombin-ATIII complex
- Heparin dramatically enhances this action

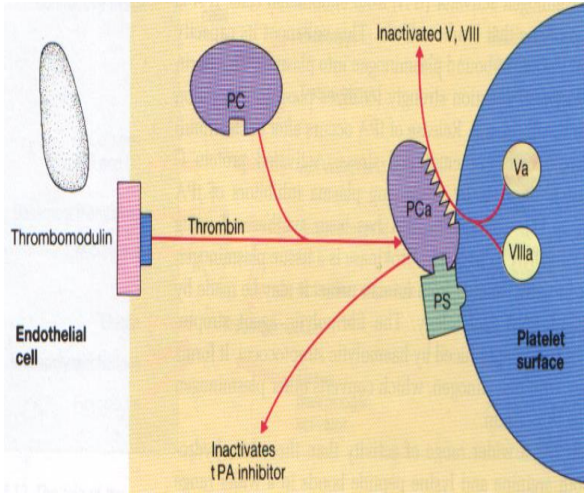
Protein C

- Synthesized by hepatocytes
- Action: inhibts **Va** & **VIIIa**
- Vitamin K-dependent

Protein S

- Cofactor for protein C

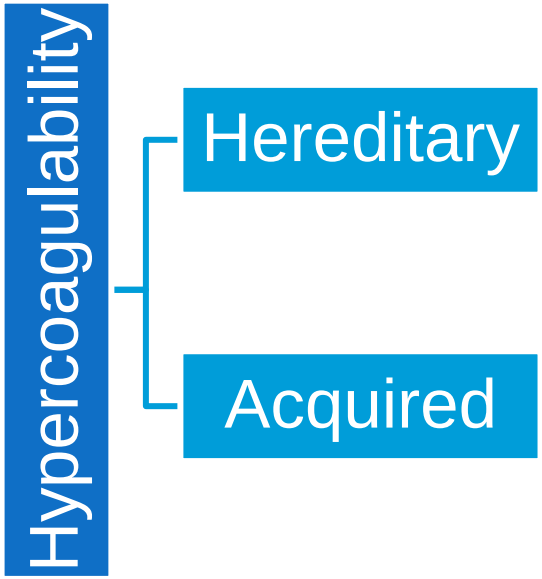
Activated protein C resistance (APC-R):
genetic abnormality of clotting factor V called **factor V Leiden mutation** (ie. Factor V becomes resistant to protein C and does not get inhibited)
labrotary test ? Functional Assay , Genetic assay



Action of Protein C & S

HYPERCOAGULABILITY

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



- Factor V Leidin
- Prothrombin G20210A
- Hyperhomocysteinaema ← د.نرفانا "ما تقلقوش نفسكو بيها"
- Deficiencies of AT III, Prot C & S
- Increased FVIII

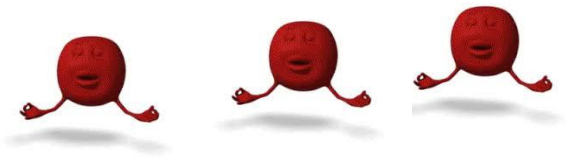
- Increase fibrinogen & FVII
- Antiphospholipid antibodies (LA & ACAs) (found in SLE patiens)
- Oestrogen therapy -smoking
- Pregnancy – dehydration Surgery and prolonged immobility - malignancy
- Major Trauma- varicose vein

Laboratory tests of hypercoagulability	
Coagulation activation markers	TAT, D-dimer, Prothrombin fraction 1+2
Genotyping	Factor V Leiden, Prothrombin G20210A, Hyperhomocysteinaemia (MTHFR)
Natural anticoagulants	ATIII, protein C, Protein S
Fibrinolysis	PAI-1, D-dimer

VIRCHOW TRIADS

Aetiological factors for thrombosis:

- ❑ Changes in blood flow (stasis) (such as immobility when someone has his leg in a cast)
- ❑ Changes in the endothelium (eg: atherosclerosis)
- ❑ Changes in blood composition(Hypercoagulability)



Summary

- 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: Tissue plasminogen activator inhibitor TPAI, 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.

MCQs

Answer key: 1:D 2:C 3:D 4: A 5:A 6: A 7:C 8:C

1- Prothrombin formation decreases in
A. Lack of Vit k
B. CNS disease
C. Liver dieses
D.A + C

2- Which of the following change fibrinogen to fibrin?
A. plasmin
B.plasminogen
C.thrombin
D.None

3- Plasmin is controlled by :
A.TPAI
B.TPA
C.Anti plasmin
D.A + C

4-Which of the following true about hemophilia ?
A. X linked disease
B. Affect female
C. Depend on vitamin K
D. A +C

5-Heparin enhance its action ?
A.ATlll
B.plasmin
C. Protein C
D.TPA

6-factor V Leiden mutation causes hypercoagulation ?
A.True
B. False

7-which of the following inactivates factor V and Vlll ?
A. Protein C
B. Endothelial Surface Factors
C.A and B
D.Heparin

8-Vitamin K Deficiency causes?
A. hepatitis
B.Liver cirrhosis
C.Bleeding
D.All of them

SAQs

Q1: what are Virchow Triads ?

Ans: any changes in 1- blood flow 2- endothelium 3- blood composition

Q2:when we use the Tissue Plasminogen Activator (TPA) ?

Ans: Tissue Plasminogen Activator (TPA) used to activate plasminogen to dissolve coronary clots

Q3:how can blood clot ting prevent in normal vascular system ?

Ans:By Endothelial surface factors, Fibrin fibers, Antithrombin III and Heparin.

Q4:what will happen in these conditions

1) Excess clotting = blocking of Blood Vessels

2) Excess fibrinolysis lead to tendency for bleeding

Thanks for checking our work

Good Luck

Done by:

Nada Alamri
Nuha alhumaidhi
Lina Aljurf