بسم الله الرحمن الرحيم

Haemostasis

Dr. Abeer Al-Ghumlas

Haemostasis

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

1. Recognize different stages of hemostasis
2. Describe formation and development of platelet
3. Describe the role of platelets in hemostasis.
4. Recognize different clotting factors
5. Describe the cascade of clotting .

Haemostasis

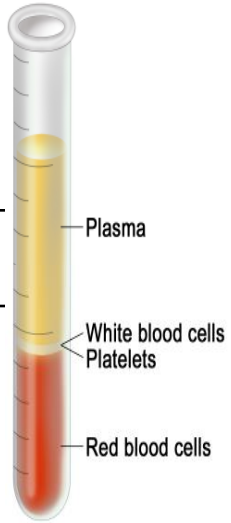
5. Describe the cascade of intrinsic pathway.
6. Describe the cascade of extrinsic and common pathways.
7. Recognize the role of thrombin in coagulation
8. Recognize process of fibrinolysis and function of plasmin

Hemostatic Mechanisms:

- **Mechanisms:**
  - Vessel wall
  - Platelet
  - Blood coagulation
  - Fibrinolytic system

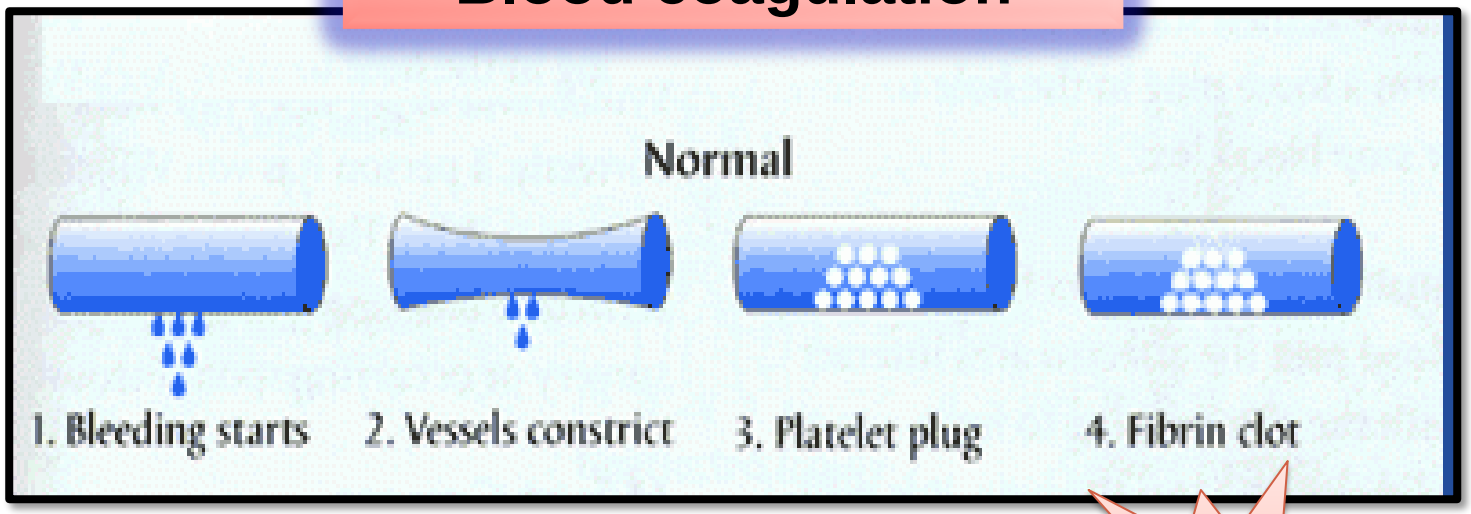
Clotting Factors

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



Circulate in plasma in inactive sate

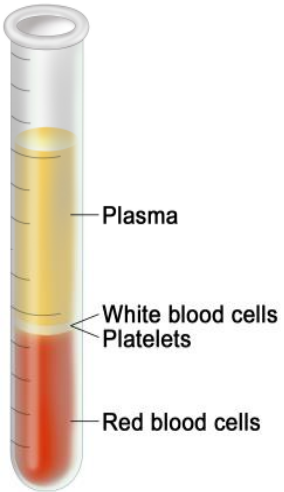
Blood coagulation

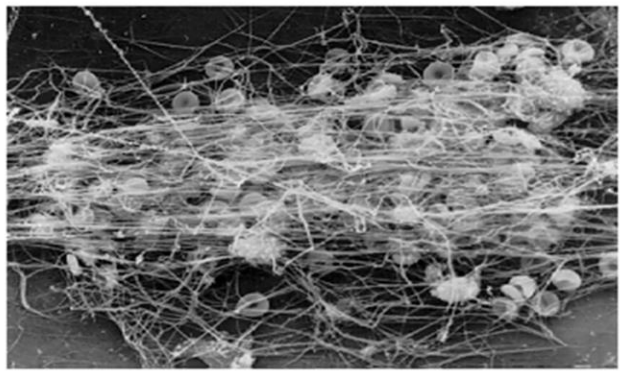


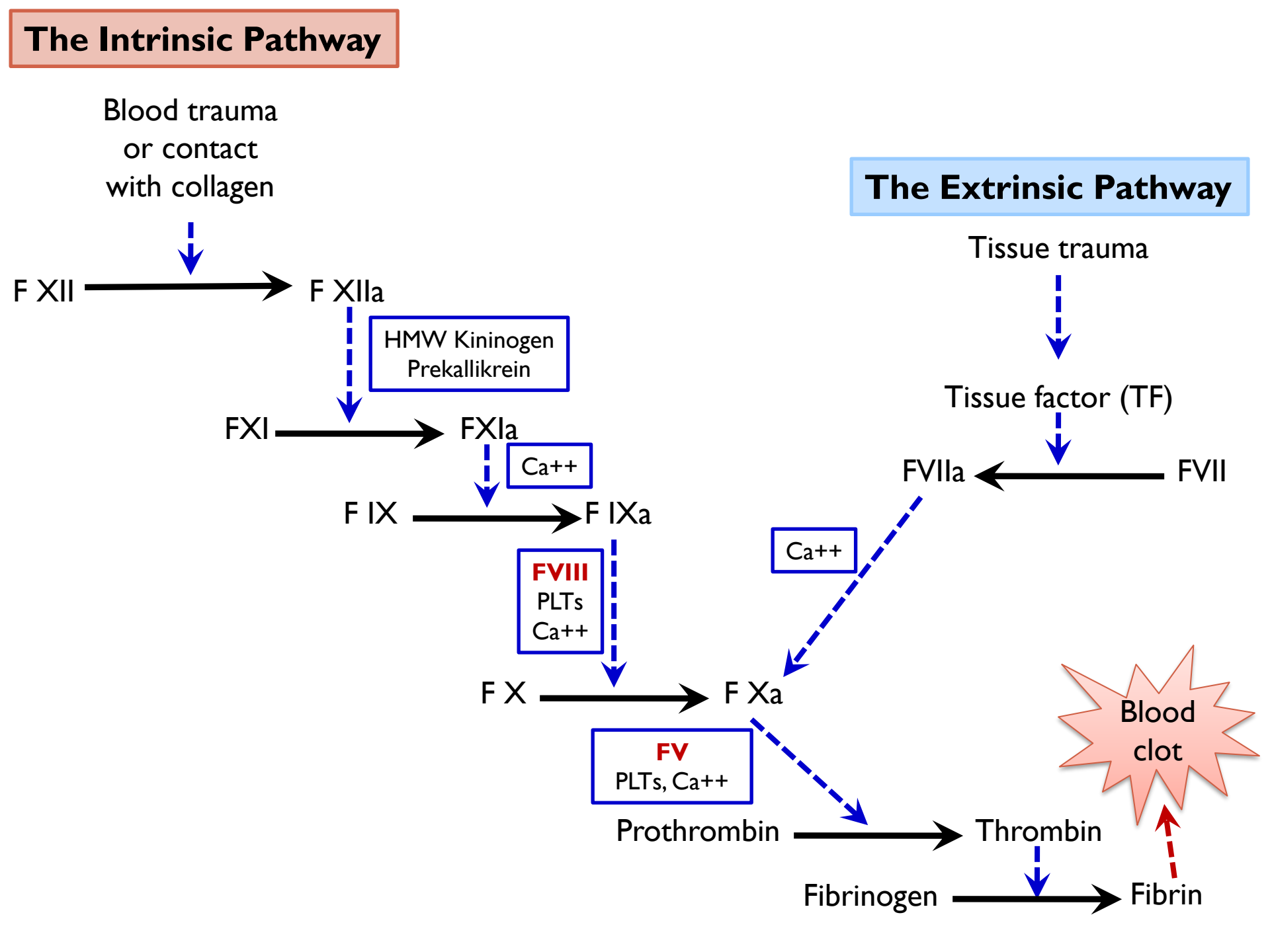
Blood clot

Thrombin

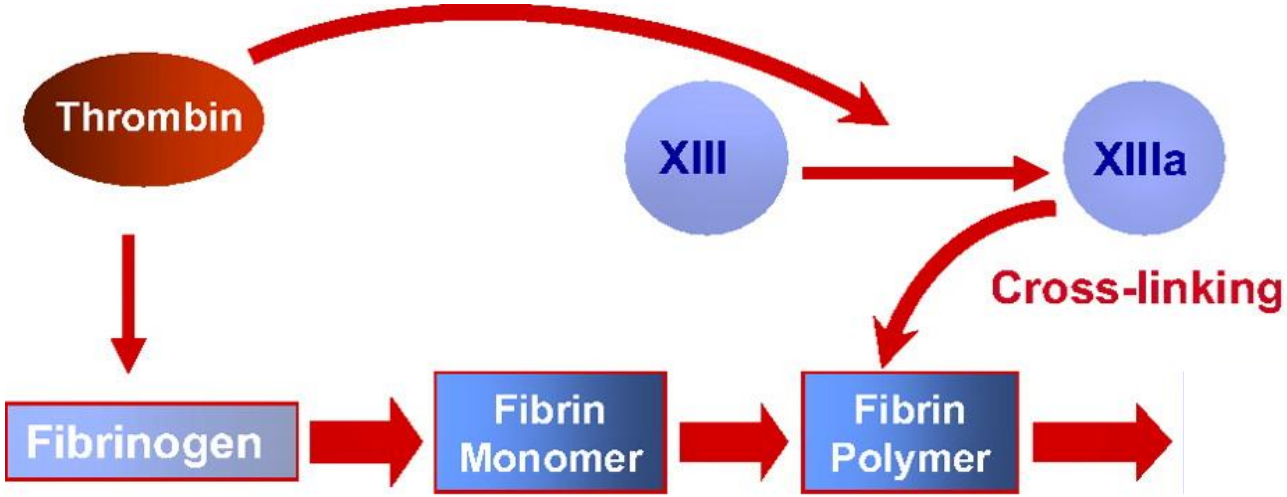
Fibrinogen → Fibrin

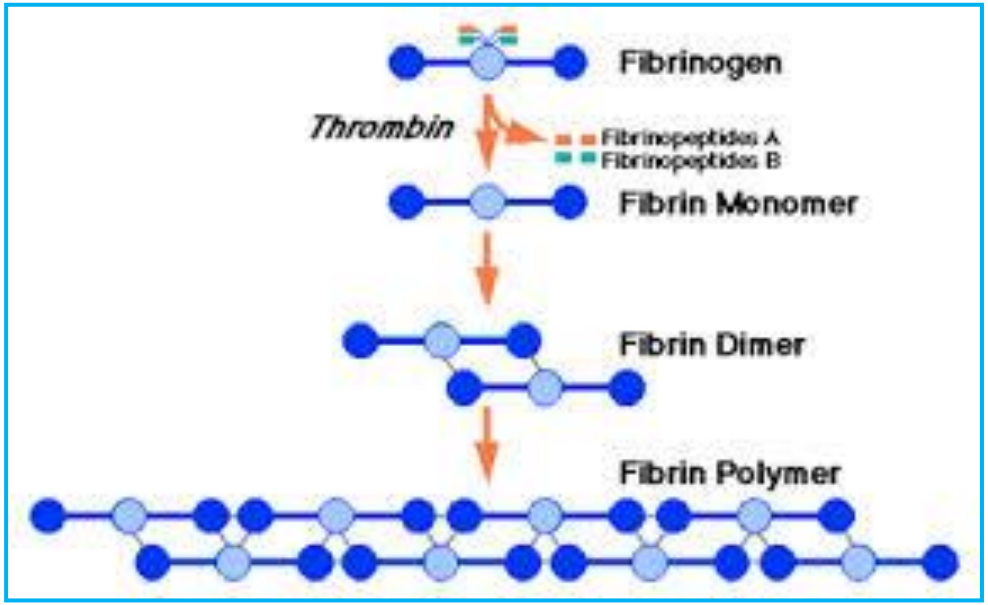





The Intrinsic Pathway
Blood trauma
or contact
with collagen
F XII
F XIIa
HMW Kininogen
Prekallikrein
FXI
FXIa
Ca++
F IX
F IXa
FVIII
PLTs
Ca++
F X
F Xa
FV
PLTs, Ca++
Prothrombin
Thrombin
Fibrinogen
Fibrin
Blood
clot
The Extrinsic Pathway
Tissue trauma
Tissue factor (TF)
FVIIa
FVII
Ca++

Blood coagulation

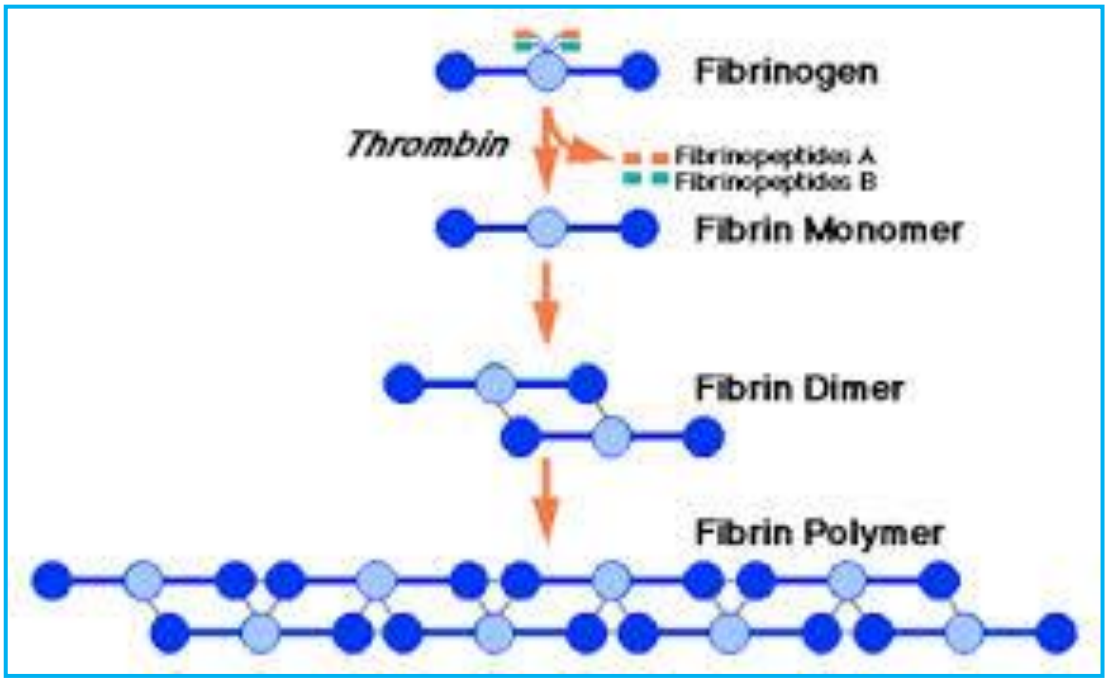


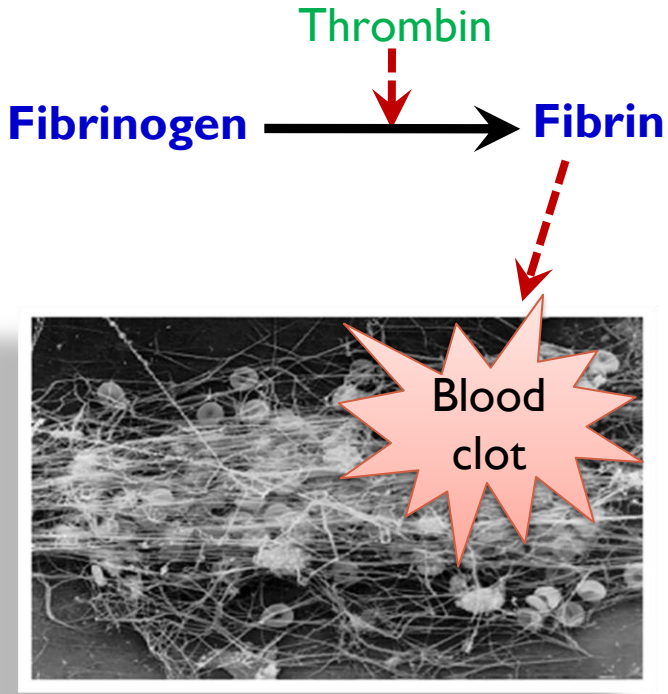


Intrinsic Pathway	Pathway Extrnsic
Contact activation ↓ XII →XIIa ↓ XI →XIa ↓ IX → IXa ↓VIII, Ca,P X → Xa	Tissue Factors ↓ ↓ ↓ ↓ VII,Ca ↓ ↓ ↓ Xa ← X

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

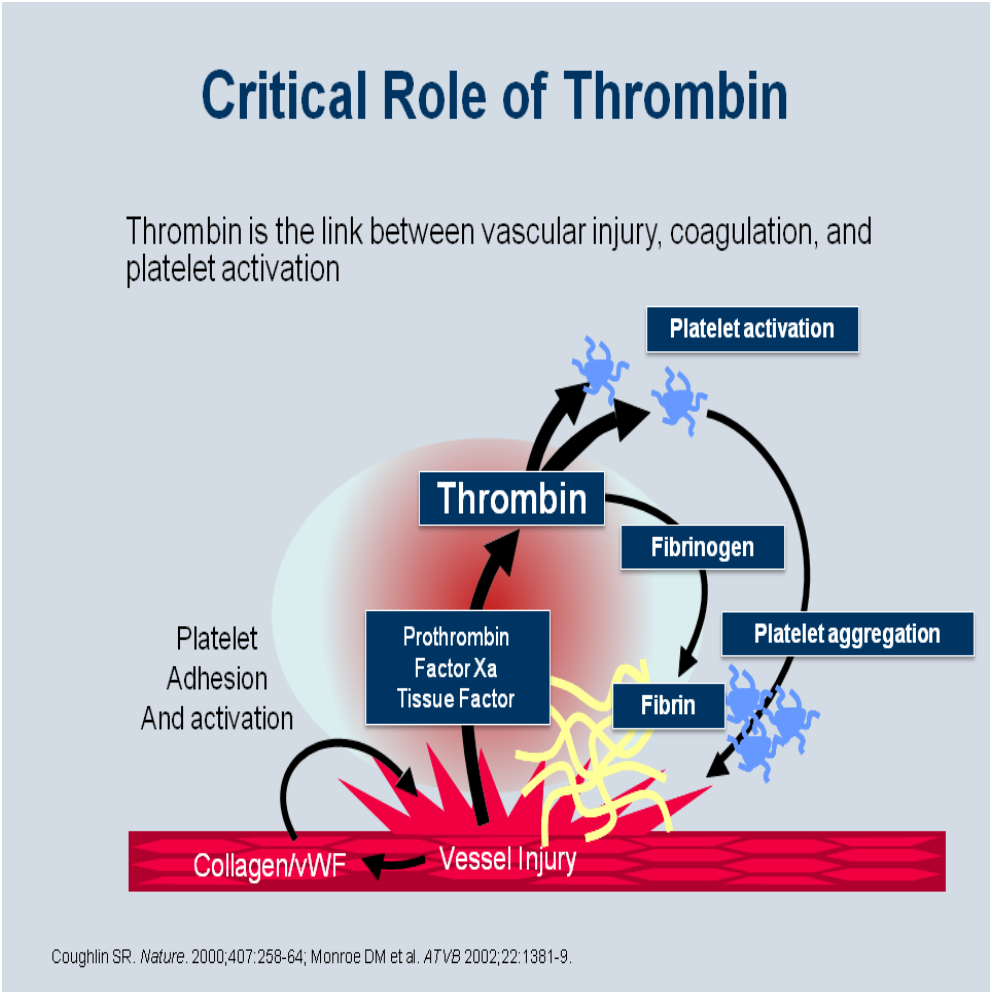
Blood coagulation





Thrombin

- Thrombin changes fibrinogen to fibrin
- Activates factor V and factor XIII
- Thrombin is essential in platelet morphological changes to form primary plug
- Thrombin stimulates platelets to release ADP & thromboxane A2; both stimulate further platelets aggregation




WEBSHOTS

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

Blood coagulation

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
- Xla will activate IX
- IXa + VIII + platelet phospholipid + Ca activate X
- Following this step the pathway is common for both

Blood coagulation

Extrinsic pathway

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

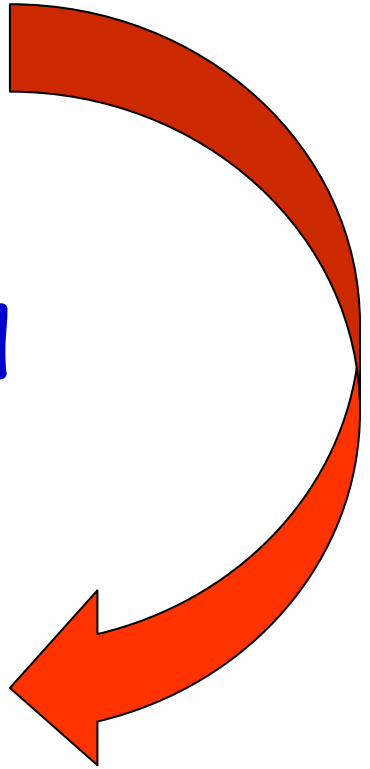
Common pathway

- Xa + V +PF3 + Ca (prothrombin activator) it is a proteolytic enzyme activate prothrombin → thrombin
- Thrombin act on fibrinogen → insoluble thread like fibrin
- Factor XIII + Ca → strong fibrin (strong clot)

Activation of Blood Coagulation

- **Intrinsic Pathway:** all clotting factors present in the blood

- **Extrinsic Pathway: triggered by tissue factor**



Common Pathway

Intrinsic Pathway

Contact activation

↓

XII →XIIa

↓

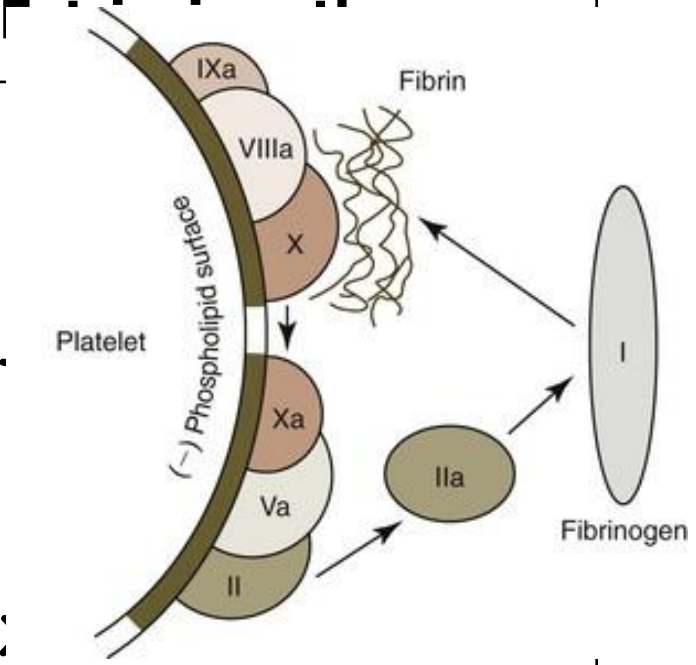
XI →XIa

↓

IX → IXa

↓**VIII, Ca,P***

X → Xa



Xa

↓

↓ **V, Ca, P***

Prothrombin (II) → Thrombin (IIa)

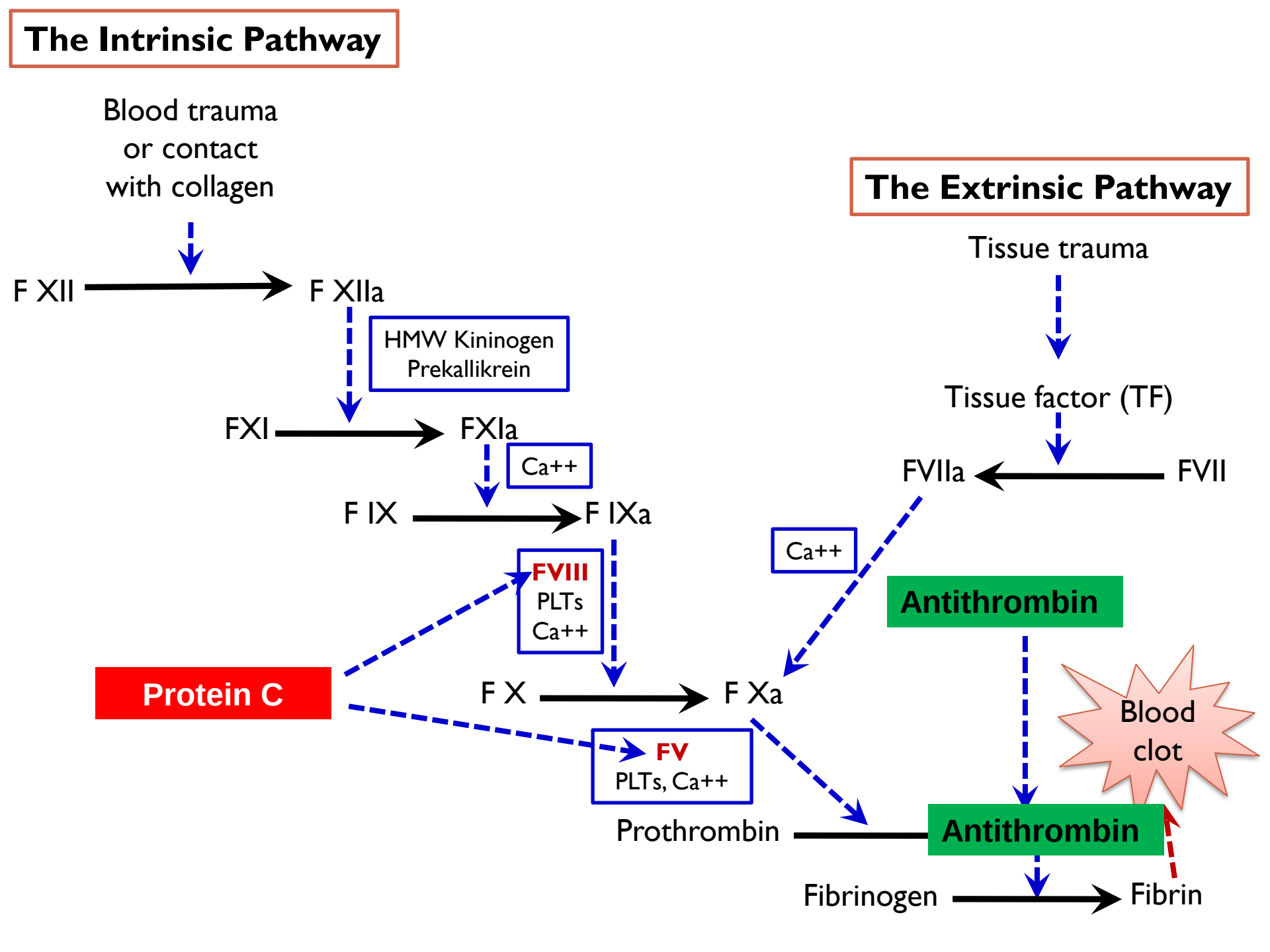
↓

Fibrinogen (I) → Fibrin (soluble)

↓ **XIII, Ca**

insoluble fibrin

P* = phospholipid from platelets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Protein C
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FV
PLTs, Ca++
Prothrombin
Antithrombin
Fibrinogen
Fibrin
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FVIIa
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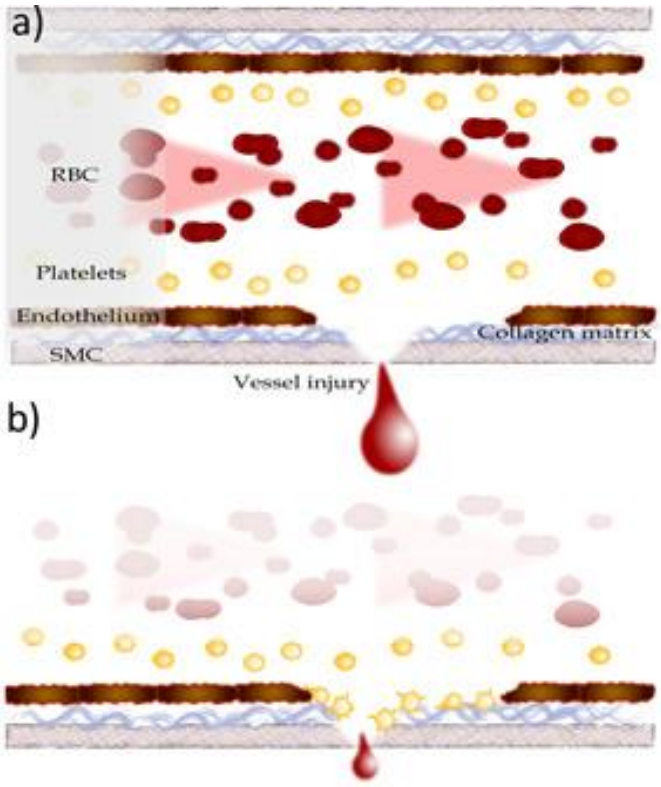
Antithrombin
Blood
clot

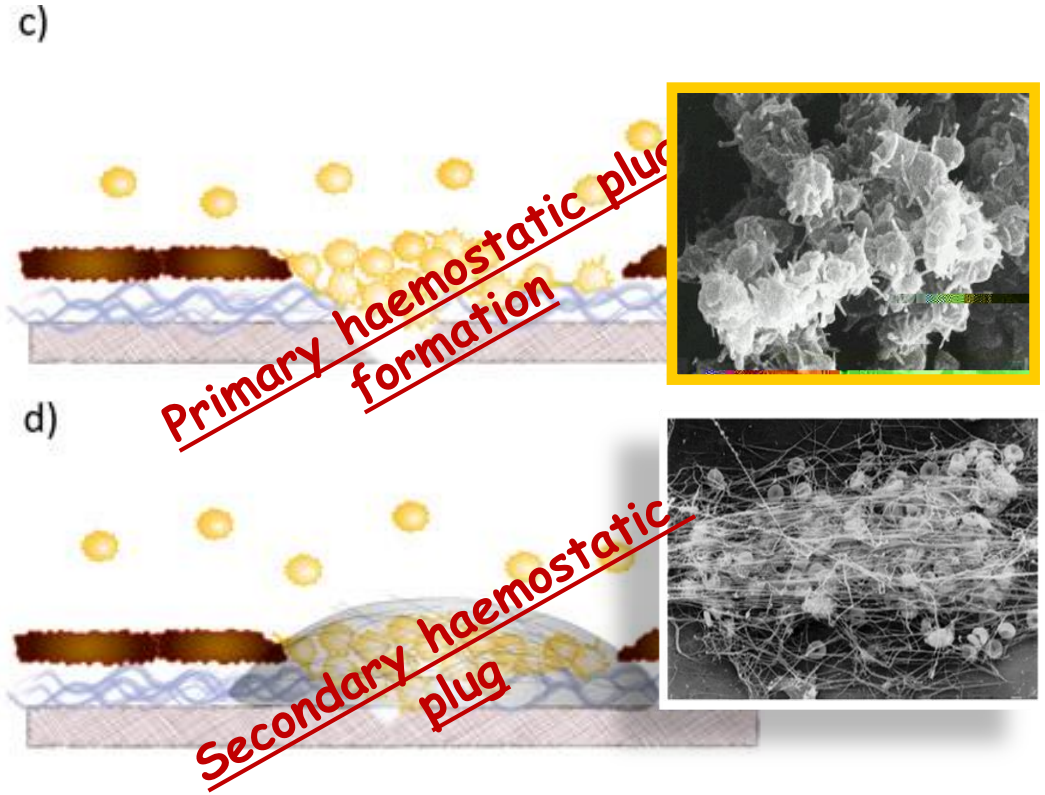
REGULATION OF COAGULATION

- Antithrombin:
  inhibits thrombin and other enzymes
- Protein C:
  degrades activated factors V and VIII
- Protein S:
  cofactor for protein C
- Tissue factor pathway inhibitor (TFPI):
  Inhibits the extrinsic system by inhibiting Factor VIIa

- Deficiency of any of these proteins can increase risk of thrombosis

Haemostasis





Hemostasis:

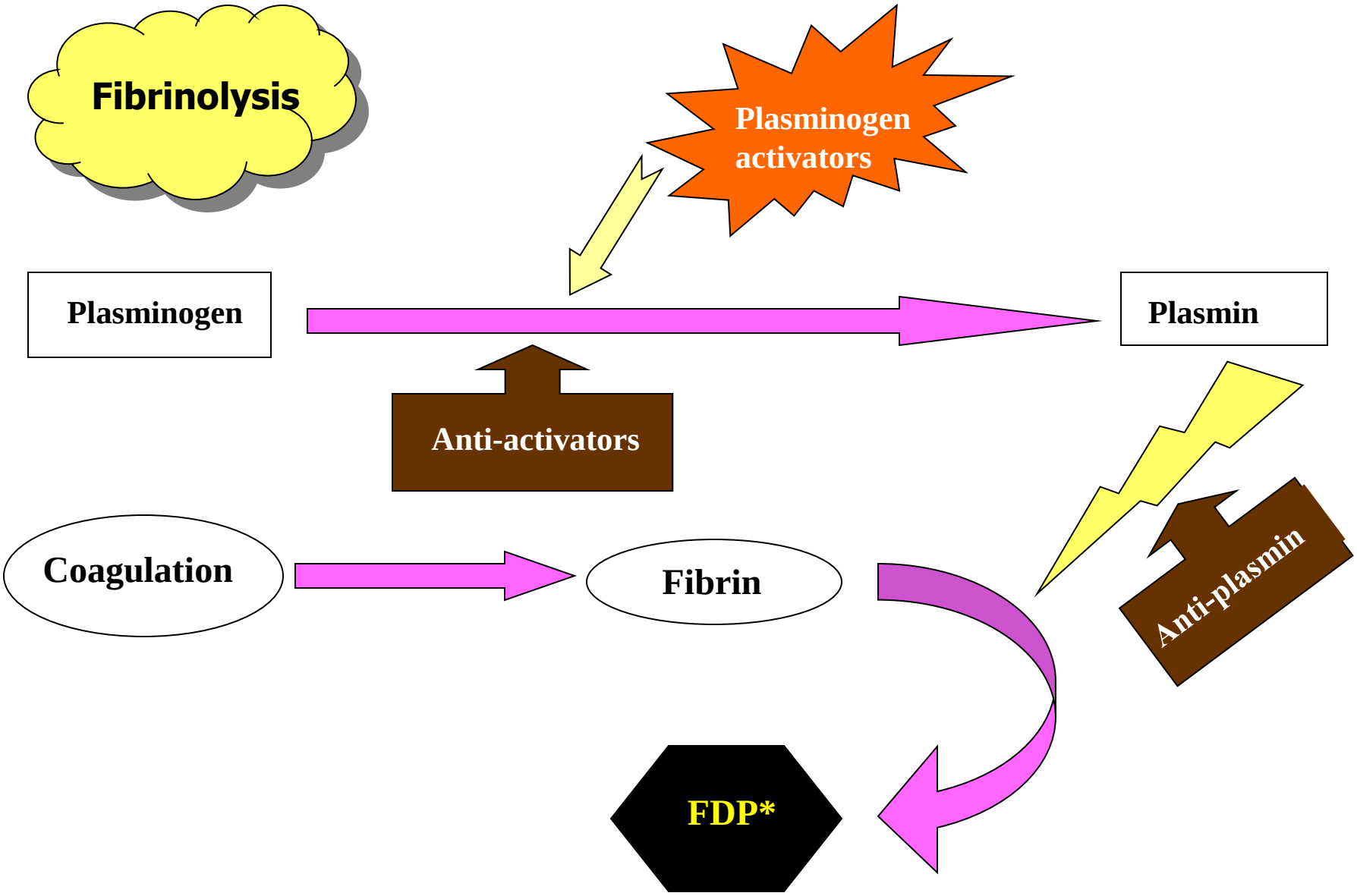
the spontaneous arrest of bleeding from ruptured blood vessels

Mechanisms:

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

Fibrinolysis

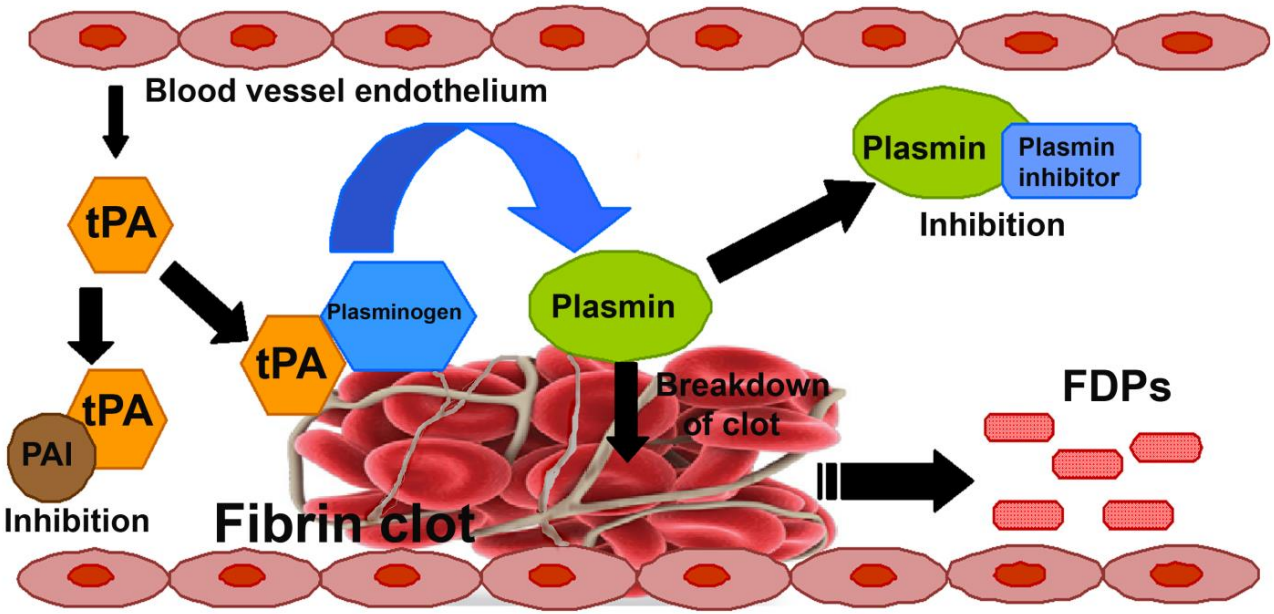
- Formed blood clot can either become fibrous or dissolve
- Fibrinolysis (dissolving) = Break down of fibrin by naturally occurring enzyme plasmin therefore prevent intravascular blocking



The fibrinolytic System

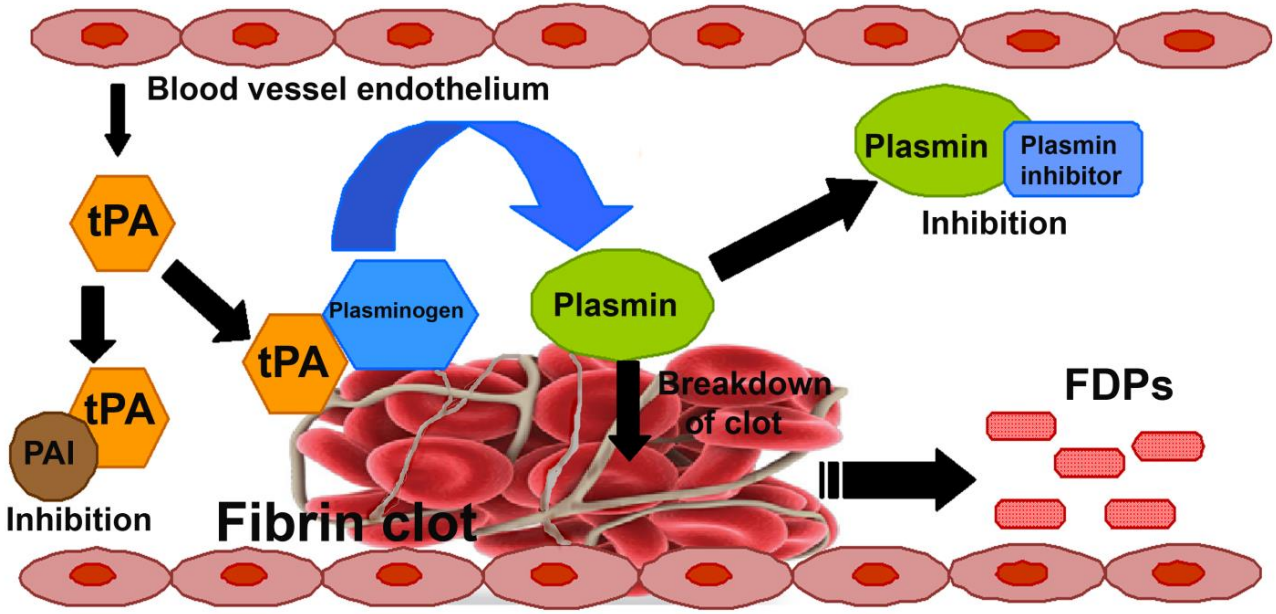
FDP*: Fibrin Degradation Products

Fibrinolysis



- 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

Fibrinolysis

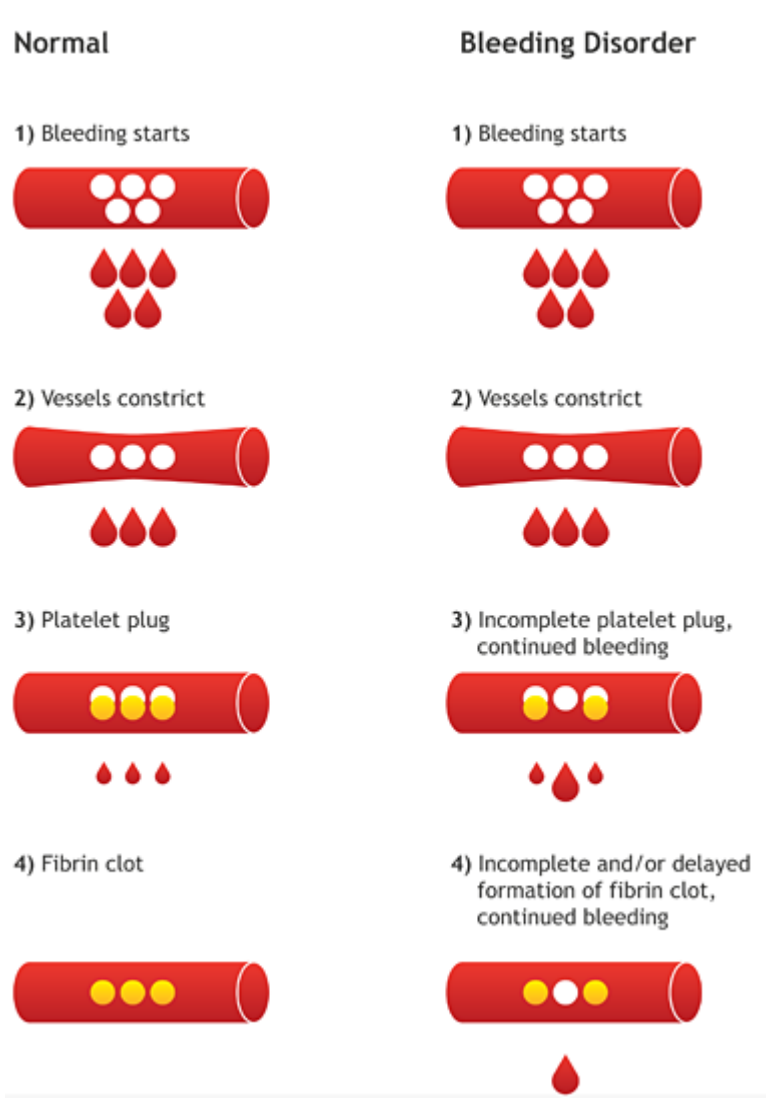


- Plasmin is controlled by:
  - Plasminogen Activator Inhibitor (PAI)
  - Antiplasmin from the liver
- Uses:
  - Tissue Plasminogen Activator (t-PA) used to activate plasminogen to dissolve coronary clots

Haemostatic Mechanisms:

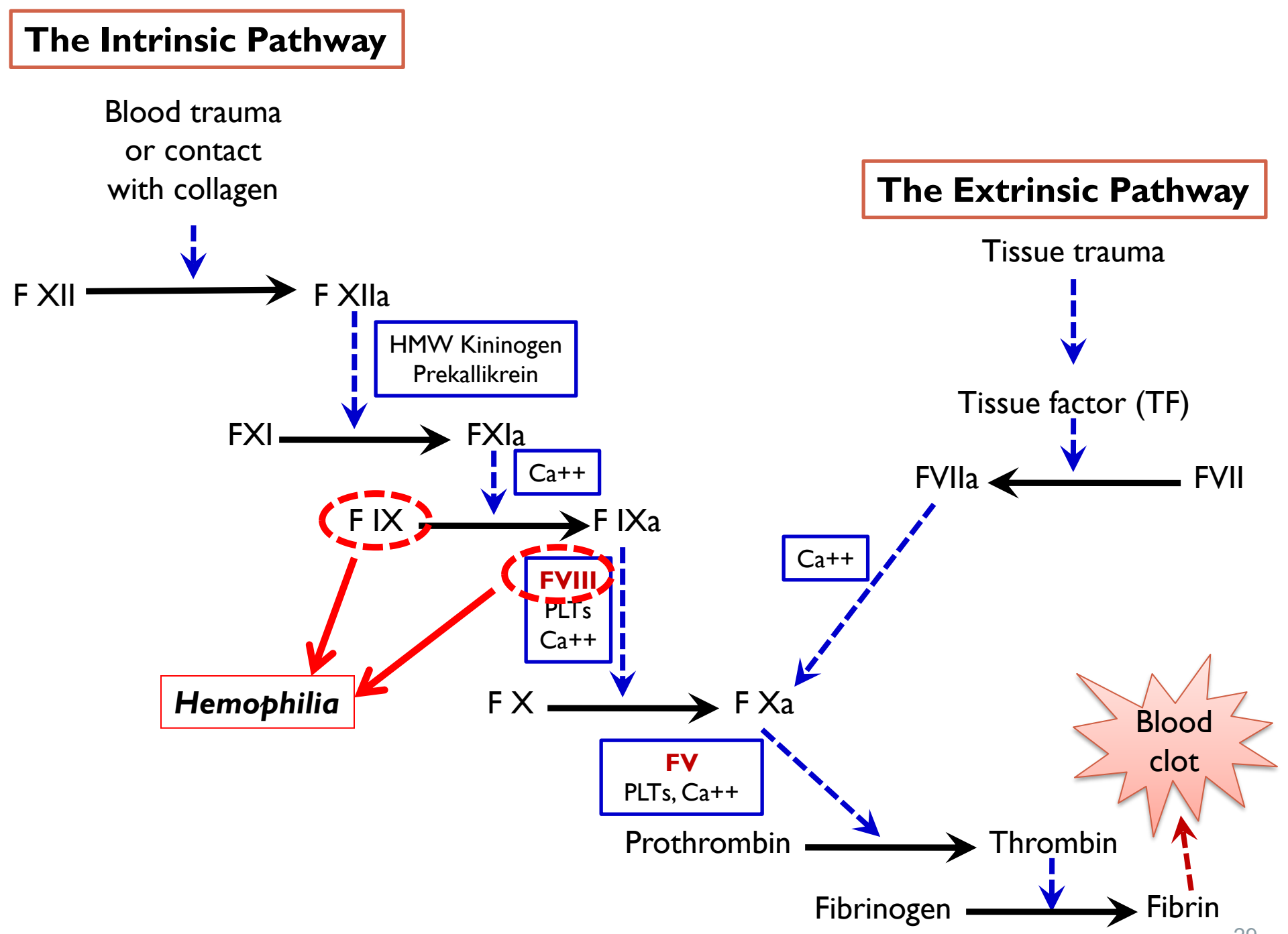
- Vessel wall
- Platelet
- Blood coagulation
- Fibrinolytic system

Bleeding disorders



- 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.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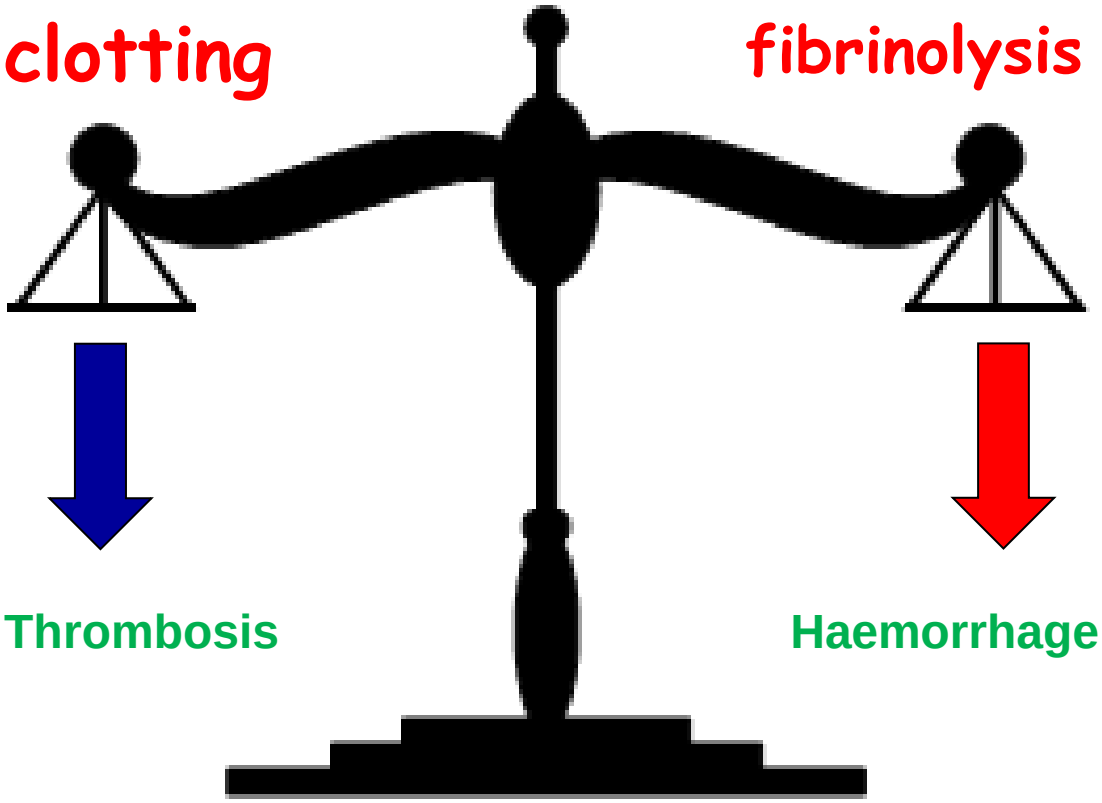
Bleeding disorders

- 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.

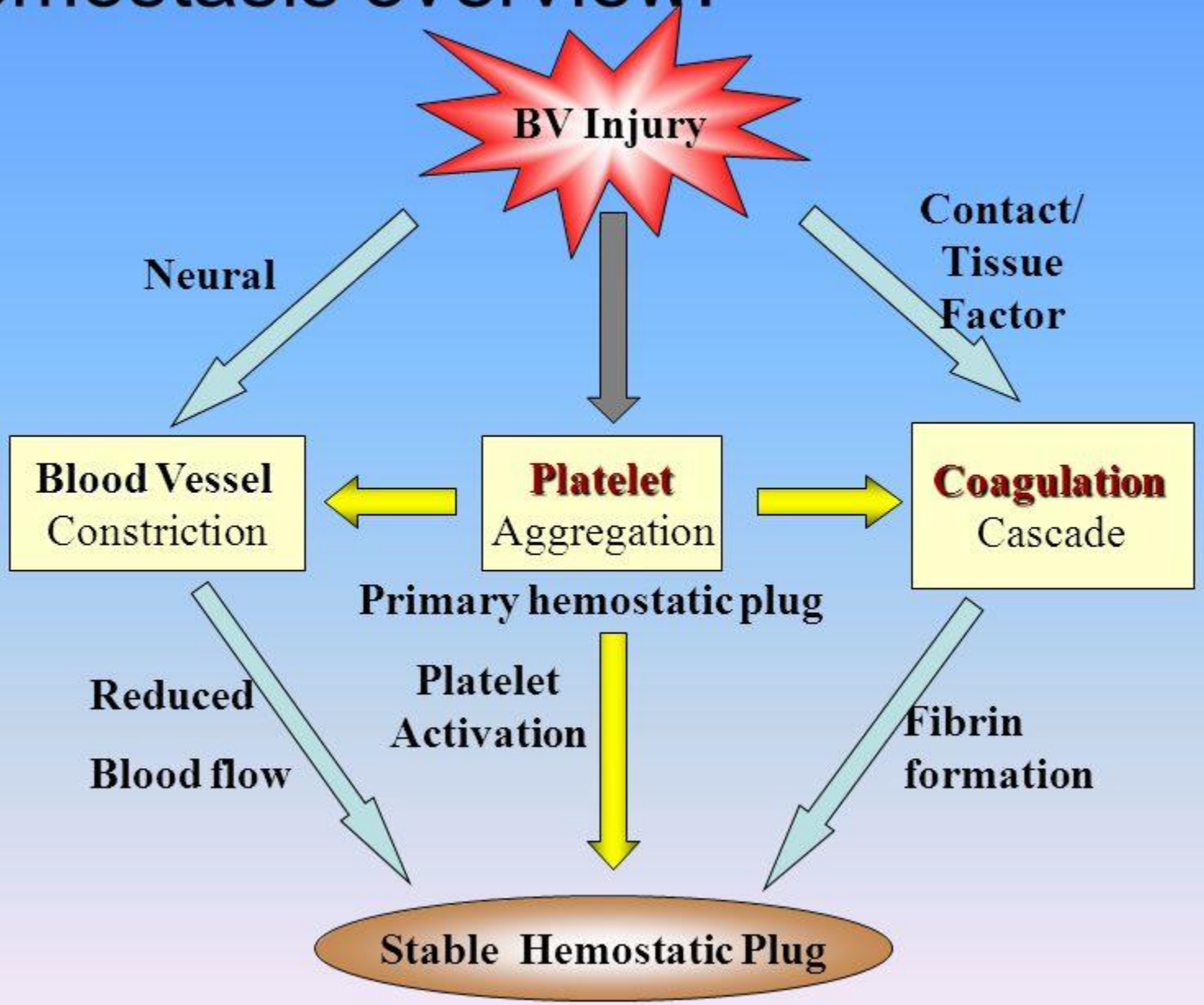


There is balance between clotting and fibrinolysis

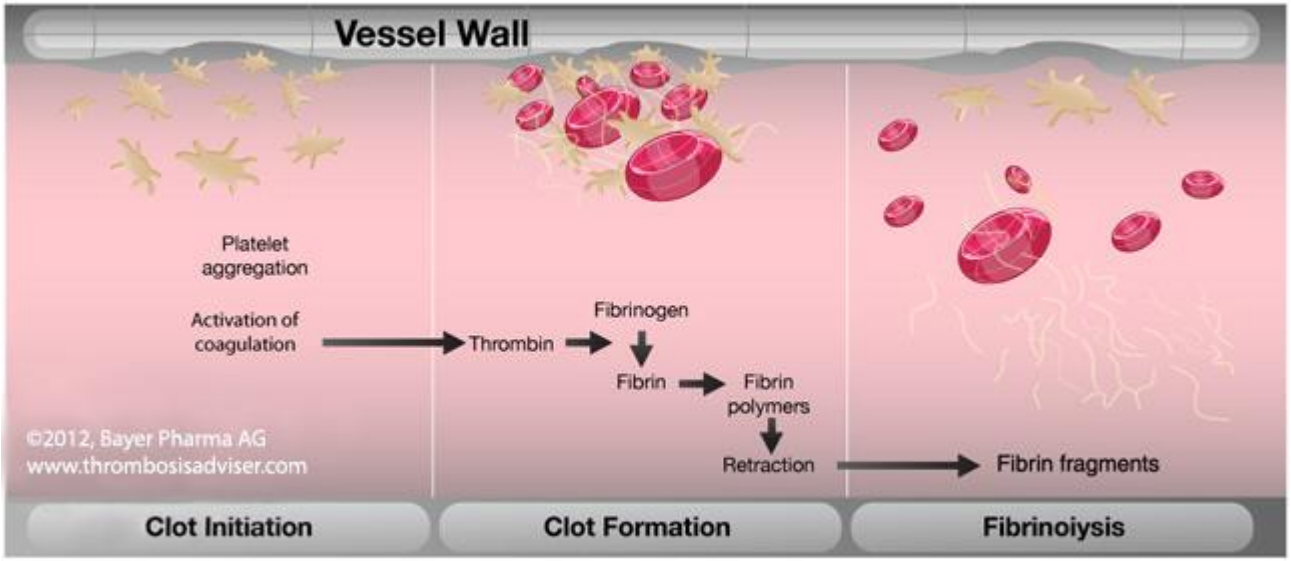
Excess clotting → blocking of Blood Vessels

Excess fibrinolysis → tendency for bleeding

Haemostasis overview:



Haemostatic Mechanisms




38 giardino privato a cittã della pieve
THANK YOU