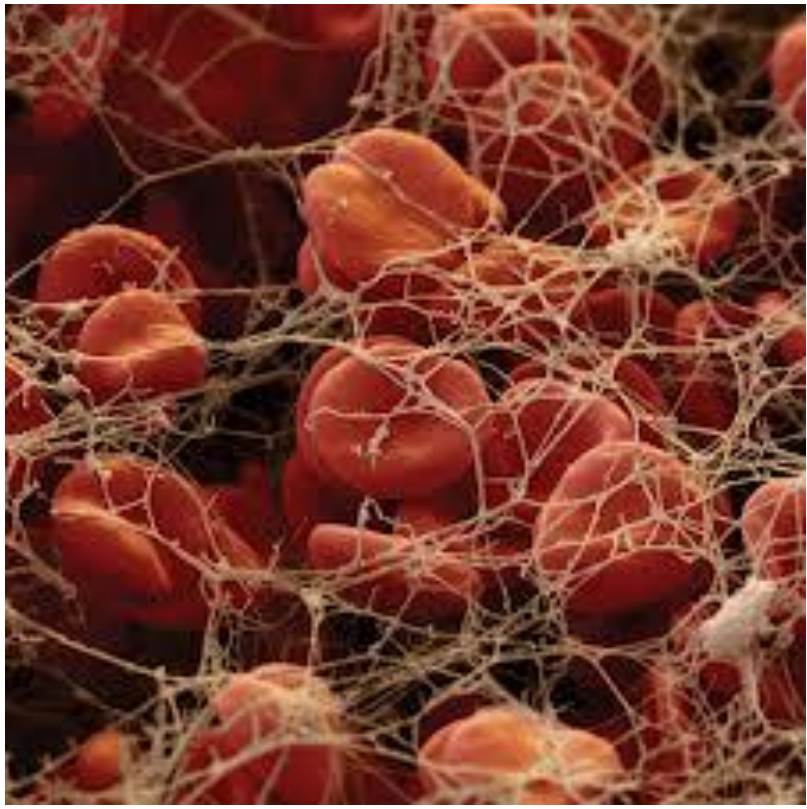
Anticoagulants

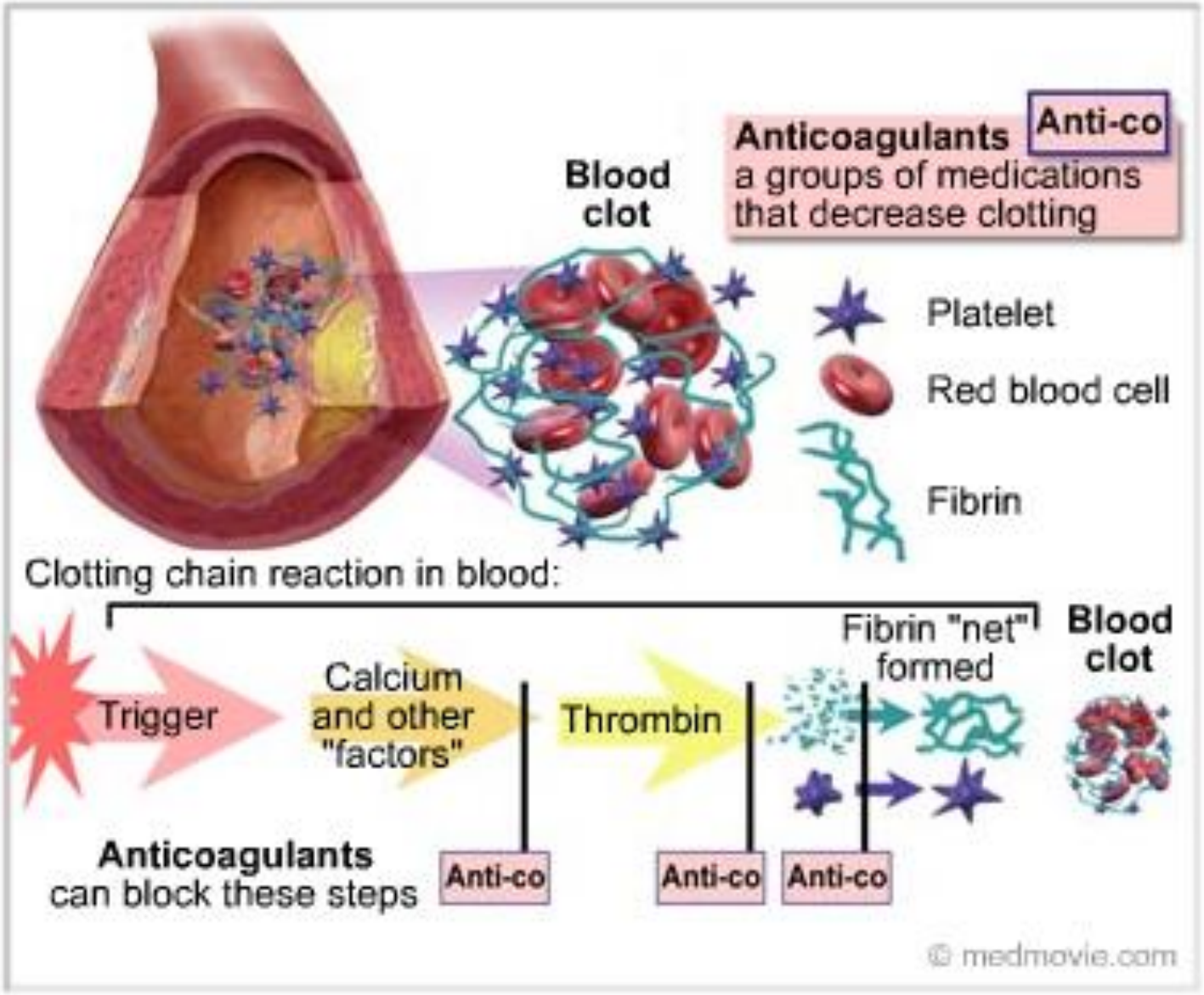


By Dr. Shaikh Fahad Falah

Learning objectives

- To know the clotting pathways and where they can be intervened.
- To know about anticoagulants; heparin and warfarin.
- Their mechanism of action.
- Common uses and contraindications.

Anticoagulants

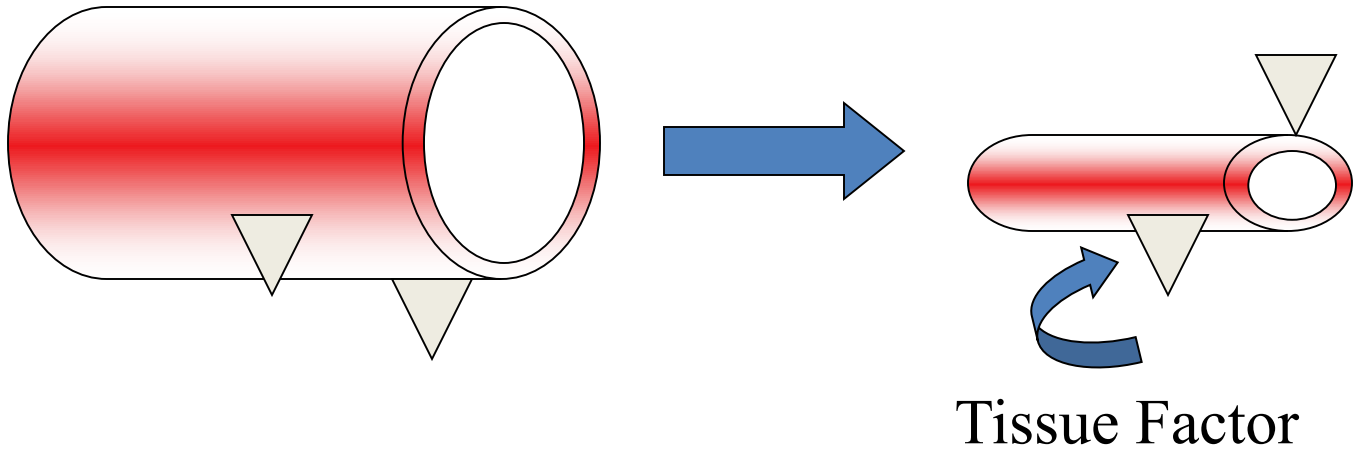


Blood Clotting

- **Vascular Phase**
- **Platelet Phase**
- **Coagulation Phase**
- **Fibrinolytic Phase**

Vascular Phase

- **Vasoconstriction**
- **Exposure to tissues activate Tissue factor and initiate coagulation**

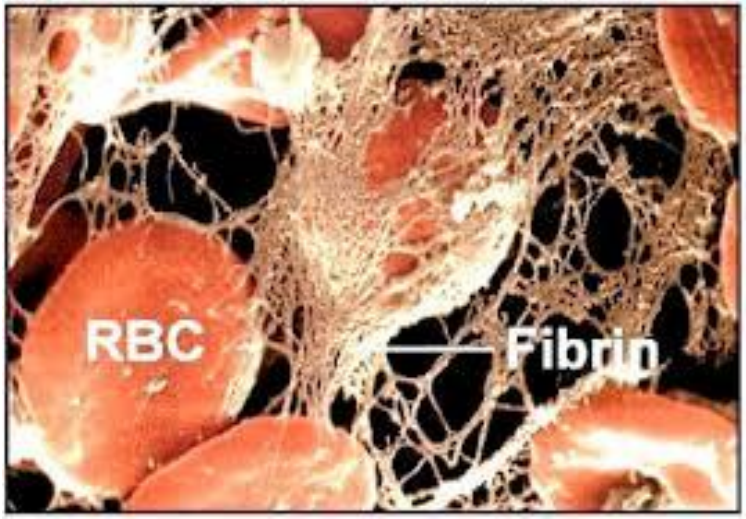


Platelet phase

- (endothelial cells) prevent platelet adhesion and aggregation
- platelets contain receptors for fibrinogen and von Willebrand factor
- after vessel injury Platelets adhere and aggregate.
- Loose their membrane and form a viscous plug

Coagulation Phase

- Two major pathways
  - Intrinsic pathway
  - Extrinsic pathway



- Both converge at a common point
- 13 soluble factors are involved in clotting

Coagulation Phase

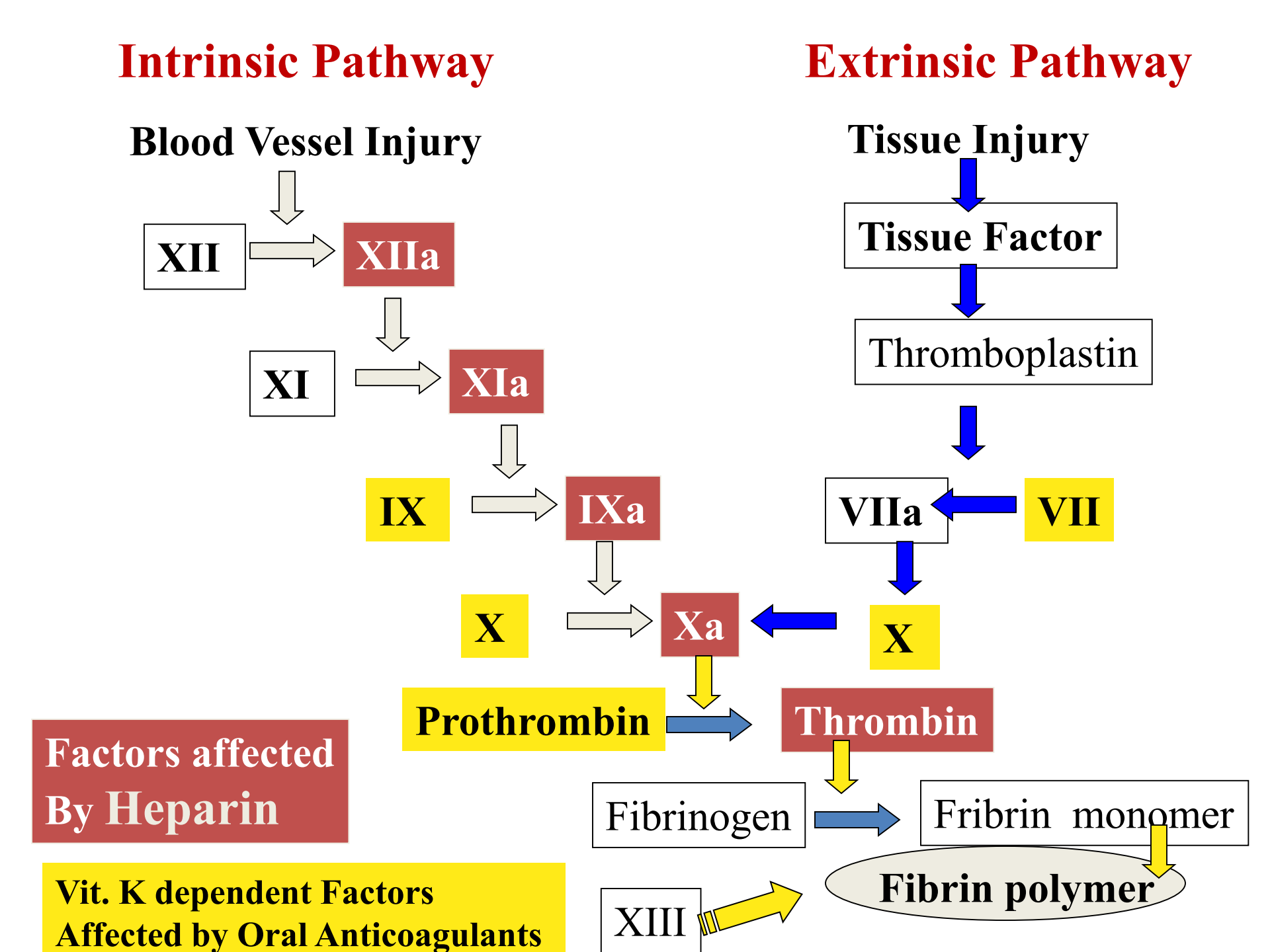
- Biosynthesis of these factors are dependent on Vitamin K1 and K2
- Normally inactive and sequentially activated
- Hereditary lack of clotting factors lead to hemophilia -A

Intrinsic Pathway

- All clotting factors are within the blood vessels
- Clotting slower
- Activated partial thromboplastin test (aPTT)

Extrinsic Pathway

- Initiating factor is outside the blood vessels - tissue factor
- Clotting - faster - in Seconds
- Prothrombin test (PT)


Intrinsic Pathway
Extrinsic Pathway
Blood Vessel Injury
Tissue Injury
XII
XIIa
Tissue Factor
Thromboplastin
XI
XIa
IX
IXa
VIIa
VII
X
Xa
X
Prothrombin
Thrombin
Factors affected
By Heparin
Fibrinogen
Fribrin monomer
Fibrin polymer
XIII
Vit. K dependent Factors
Affected by Oral Anticoagulants

Anticoagulant drugs to treat thromboembolism

Drug Class	Prototype	Action	Effect
Anticoagulant Parenteral	**Heparin**	Inactivation of clotting Factors	Prevent venous Thrombosis
Anticoagulant Oral	**Warfarin**	Decrease synthesis of Clotting factors	Prevent venous Thrombosis
Antiplatelet drugs	**Aspirin**	Decrease platelet aggregation	Prevent arterial Thrombosis
Thrombolytic Drugs	**Streptokinase**	Fibinolysis	Breakdown of thrombi

Uses

- Acute myocardial infarction
- Arterial and venous thrombosis
- Pulmonary embolism

Contra indications

- Stroke
- Major surgery
- Brain neoplasm
- Active bleed

Heparin

A polymer of varying chain size

- **Mechanism of action**
- binds to the enzyme inhibitor antithrombin III (AT), causing a conformational change that results in its activation
- The activated AT then inactivates thrombin, factor Xa and other proteases

Administration

- given parenterally because it is not absorbed from the gut. (intravenously or subcutaneously (under the skin)intramuscular injections (into muscle) are avoided because of the potential for forming hematomas
- short biologic half-life of about one hour, heparin must be given frequently or as a continuous infusion.
- often used only to commence anticoagulation therapy until an oral anticoagulant e.g. warfarin takes effect

Warfarin

- **Warfarin**, sold under the brand name **Coumadin**
- **Mechanism of action**

inhibits the vitamin K-dependent synthesis of biologically active forms of the clotting factors II, VII, IX and X

Administration

- Warfarin is available orally. Warfarin has a long half-life and need only be given once a day

- It takes several days for warfarin to reach the therapeutic effect

Thank you