

# Coagulation Cascade - Physiology of Hemostasis

[Coagulation Cascade Animation - Physiology of Hemostasis.mp4](#)

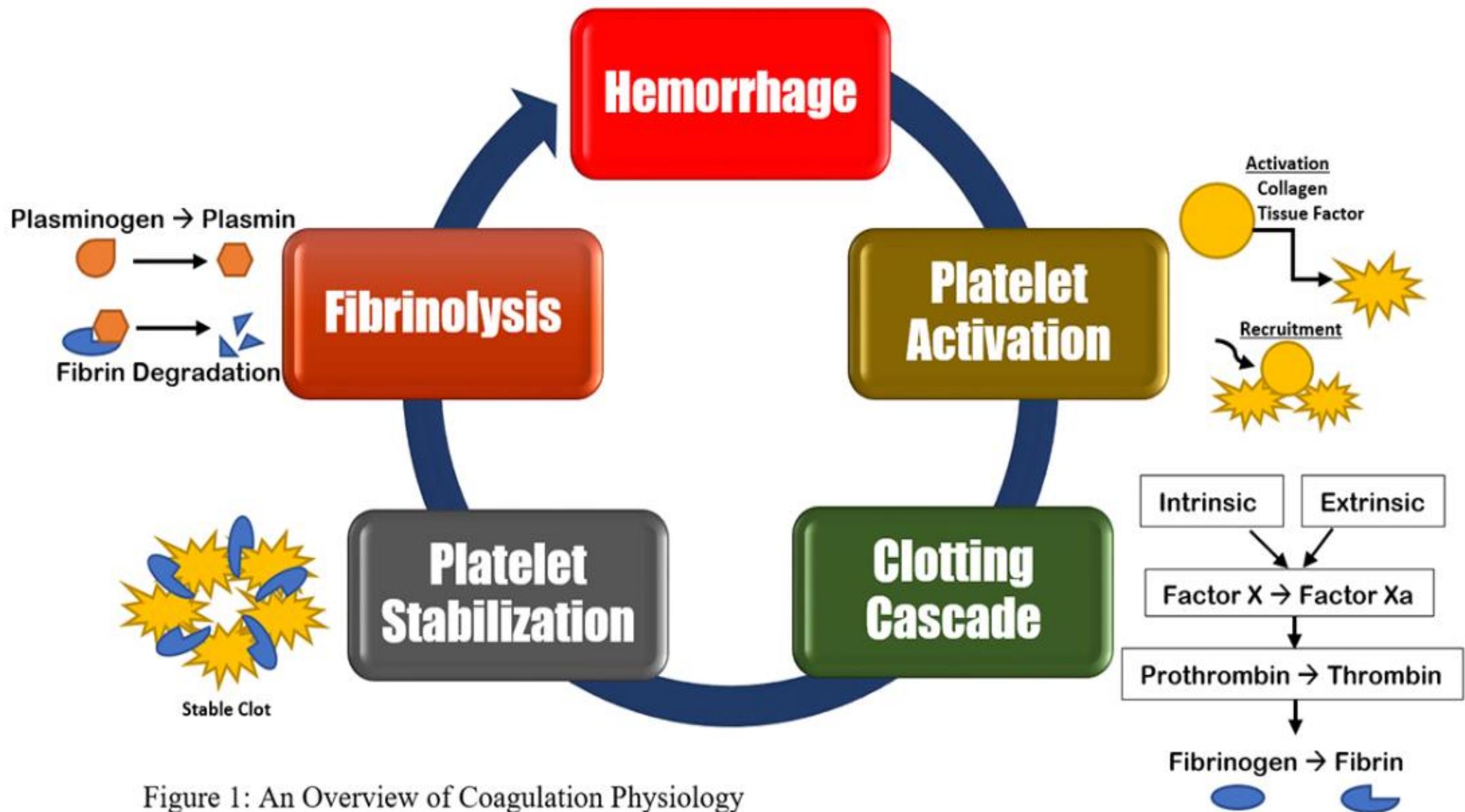


Figure 1: An Overview of Coagulation Physiology

**Table 3: Nomenclature of the coagulation proteins/clotting factors**

<b>Clotting factor number</b>	<b>Clotting factor name</b>	<b>Function</b>	<b>Plasma half-life (h)</b>	<b>Plasma concentration (mg/L)</b>
I	Fibrinogen	Clot formation	90	3000
II	Prothrombin	Activation of I, V, VII, VIII, XI, XIII, protein C, platelets	65	100
III	TF	Co factor of VIIa	-	-
IV	Calcium	Facilitates coagulation factor binding to phospholipids	-	-
V	Proacclerin, labile factor	Co-factor of X-prothrombinase complex	15	10
VI	Unassigned			
VII	Stable factor, proconvertin	Activates factors IX, X	5	0.5
VIII	Antihaemophilic factor A	Co-factor of IX-tenase complex	10	0.1
IX	Antihaemophilic factor B or Christmas factor	Activates X: Forms tenase complex with factor VIII	25	5
X	Stuart-Prower factor	Prothrombinase complex with factor V: Activates factor II	40	10
XI	Plasma thromboplastin antecedent	Activates factor IX	45	5
XII	Hageman factor	Activates factor XI, VII and prekallikrein		-
XIII	Fibrin-stabilising factor	Crosslinks fibrin	200	30
XIV	Prekallikerin (F Fletcher)	Serine protease zymogen	35	
XV	HMWK- (F Fitzgerald)	Co factor	150	
XVI	vWf	Binds to VIII, mediates platelet adhesion	12	10 µg/mL
XVII	Antithrombin III	Inhibits IIa, Xa, and other proteases	72	0.15-0.2 mg/mL
XVIII	Heparin cofactor II	Inhibits IIa	60	-
XIX	Protein C	Inactivates Va and VIIIa	0.4	-
XX	Protein S	Cofactor for activated protein C		-

# Coagulation pathway

Intrinsic pathway

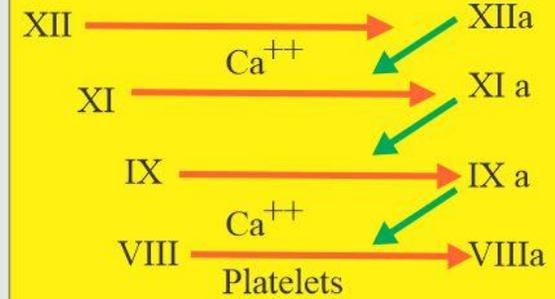
Extrinsic pathway

Initiated by

Initiated by

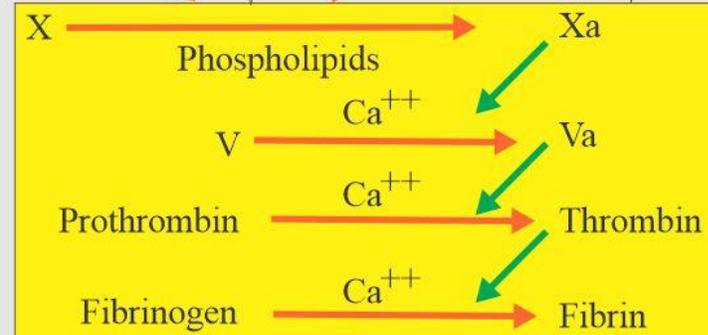
Injury in the vascular endothelium  
This is slower and more important

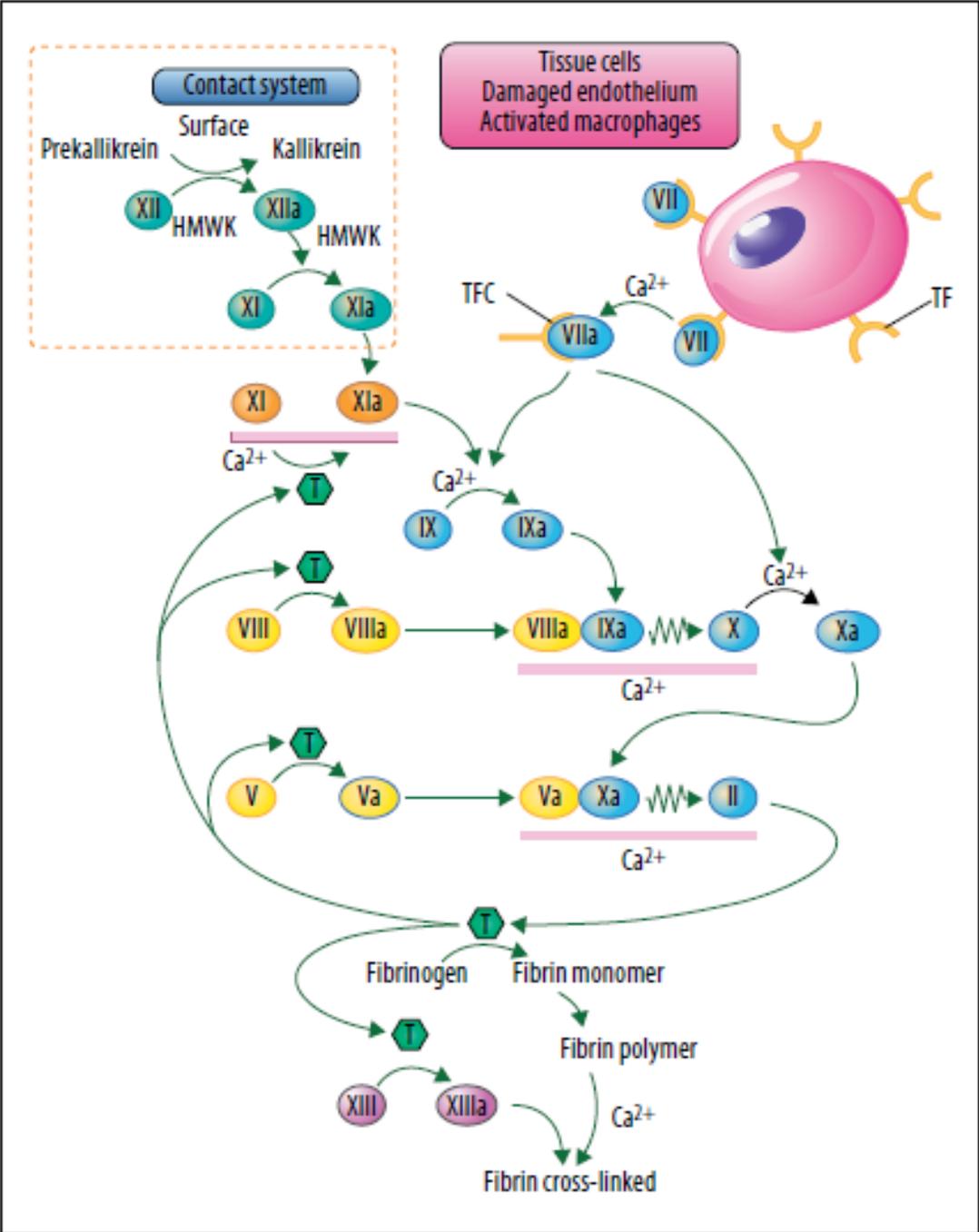
External injury



Tissue thromboplastin  
 $Ca^{++} + VII$

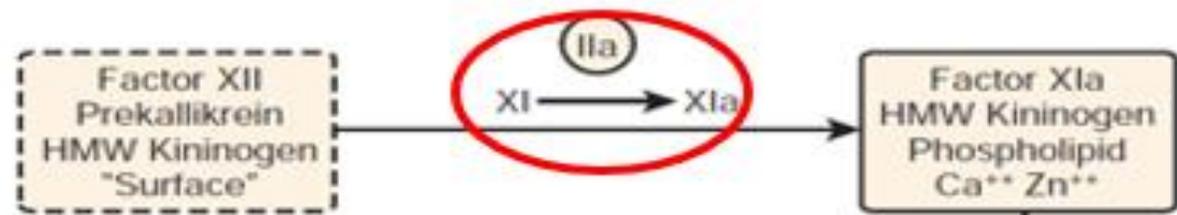
Common Pathway



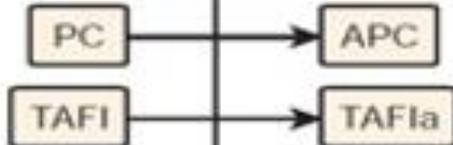
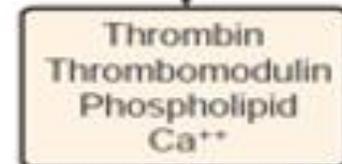
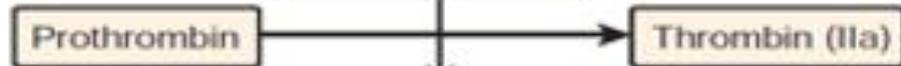
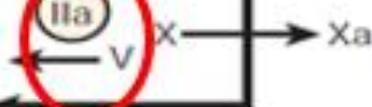
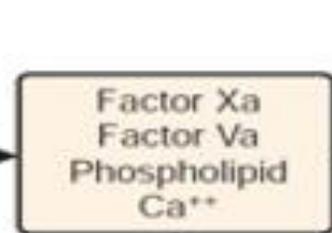
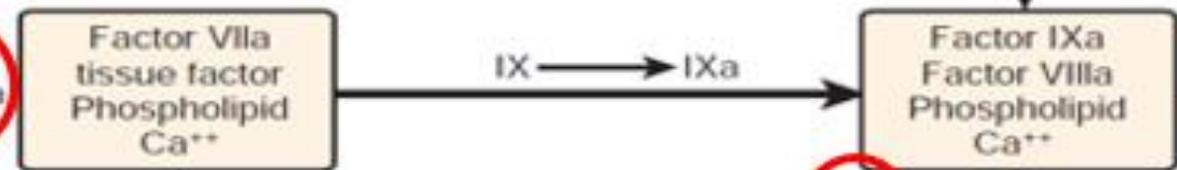
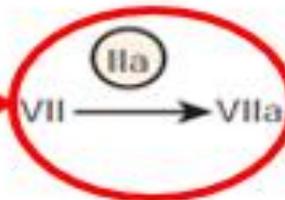


# Prothrombin Roles

Intrinsic Pathway →

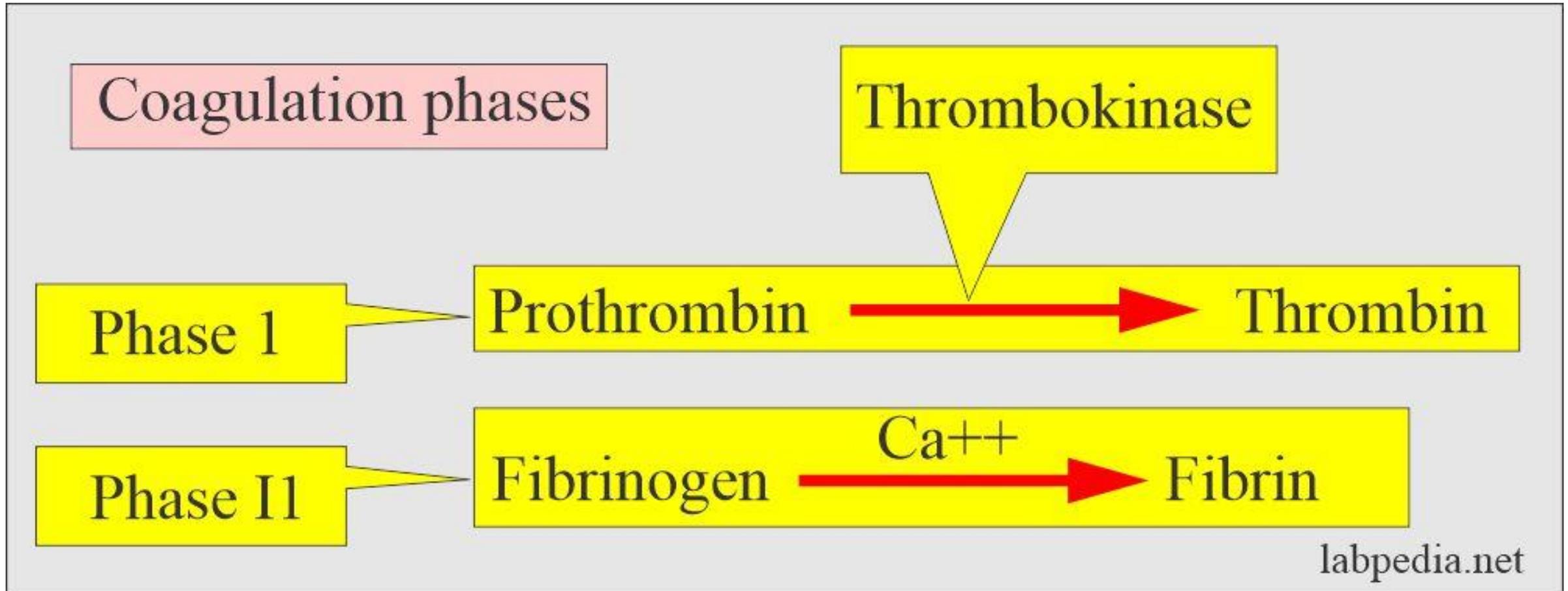


Extrinsic Pathway →



# Summary of the Coagulation process

In 1905-1906, Morowitz published the theory of blood coagulation. This was unchanged for 40 years. He divided coagulation into two phases.



# Modern theory of blood coagulation-three stages

## Coagulation modern theory

Stage 1

Generation of thromboplastin activity  
(Extrinsic and intrinsic pathway)

Stage II

Conversion of prothrombin to thrombin

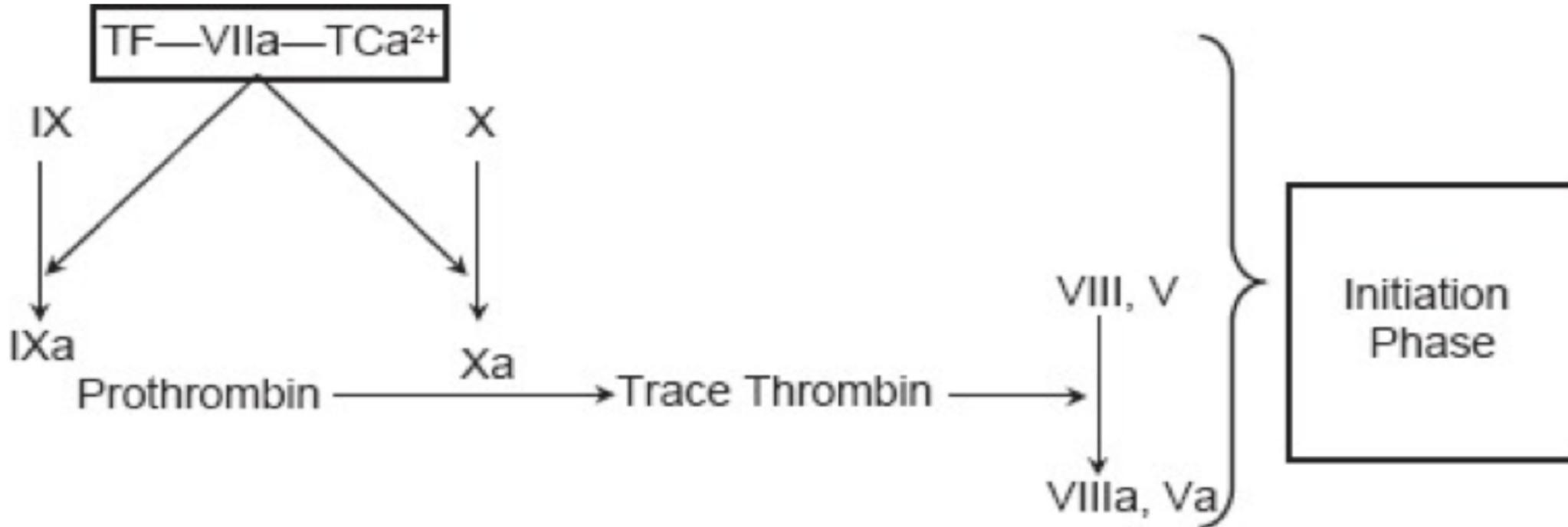
Stage III

Conversion of fibrinogen to fibrin by thrombin

# Xase of extrinsic factor

## Current Concept of Coagulation

Current evidence supports the understanding that intrinsic pathway is not a parallel pathway but indeed it augments thrombin generation primarily initiated by the extrinsic pathway (19).



**Figure 5.** Current concept of coagulation (initiation phase).

# Xase of Intrinsic factor

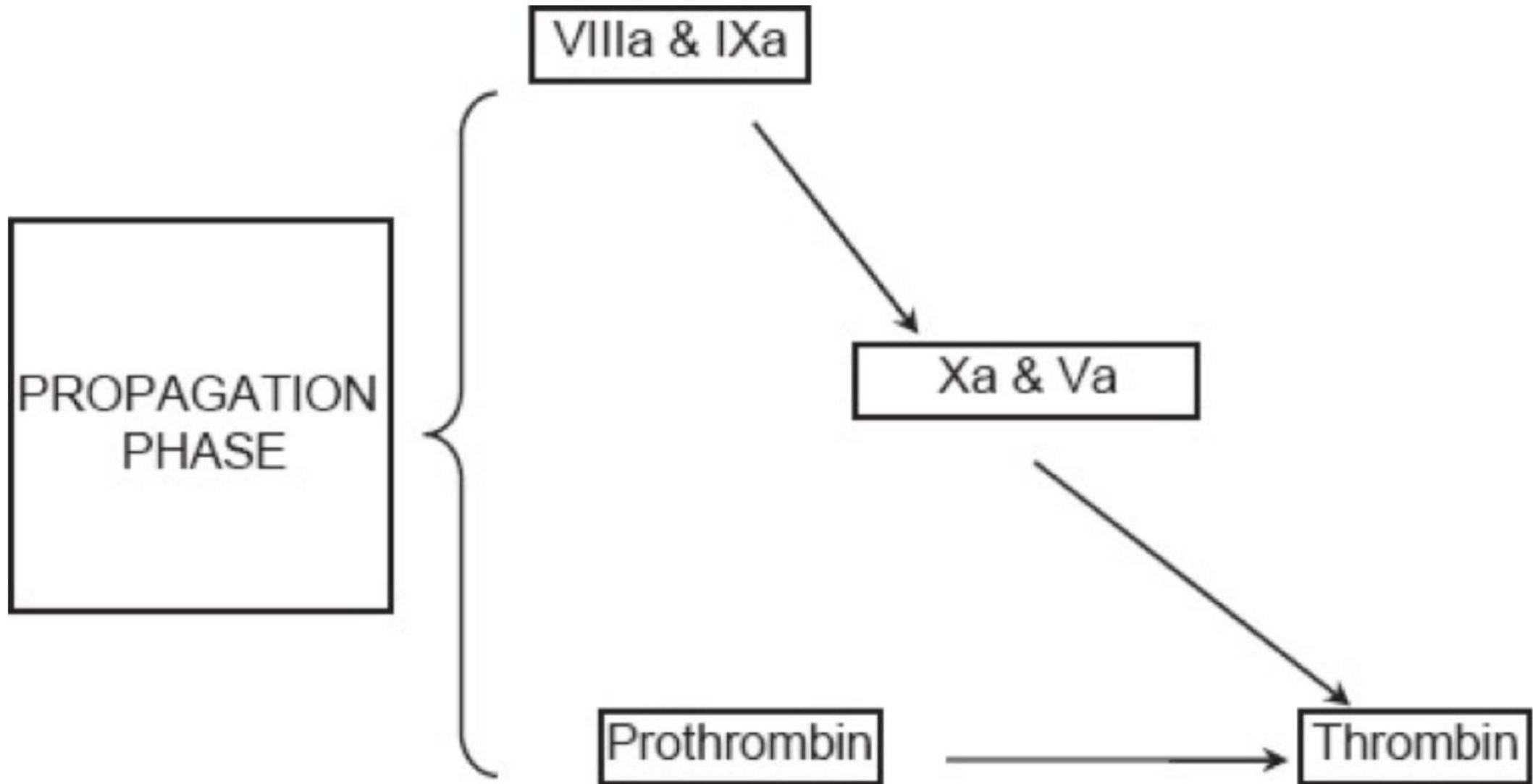
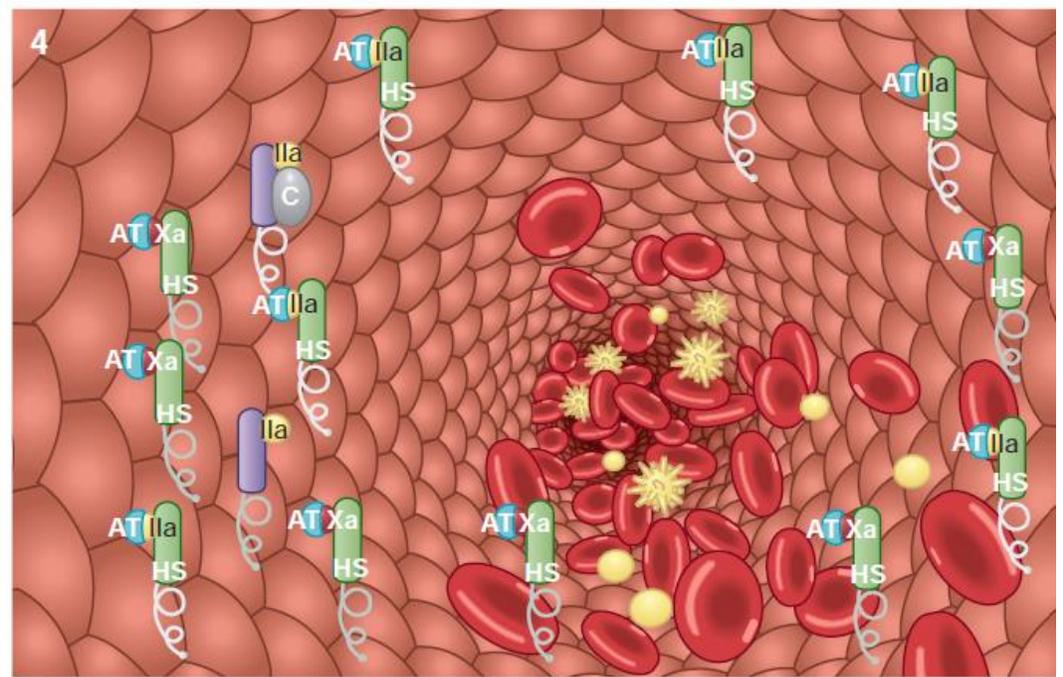
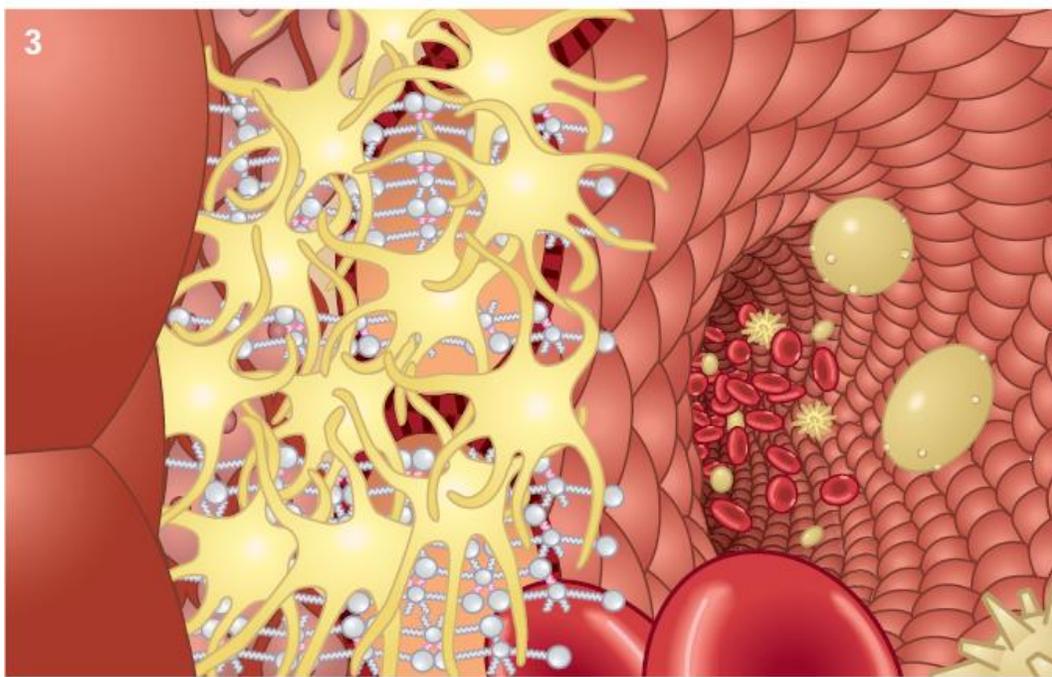
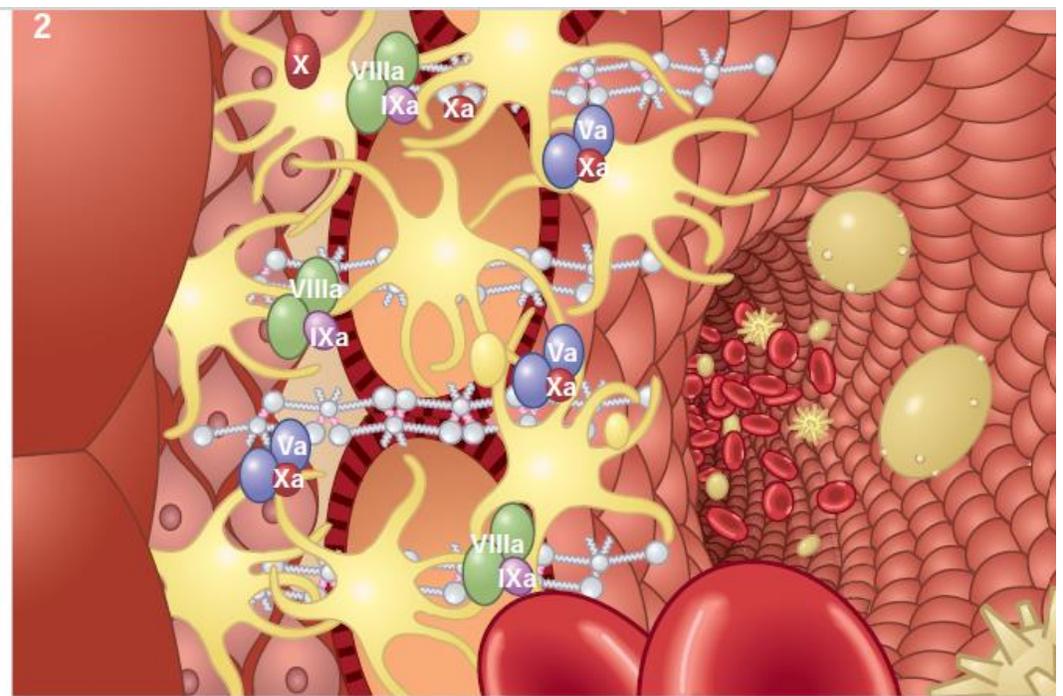
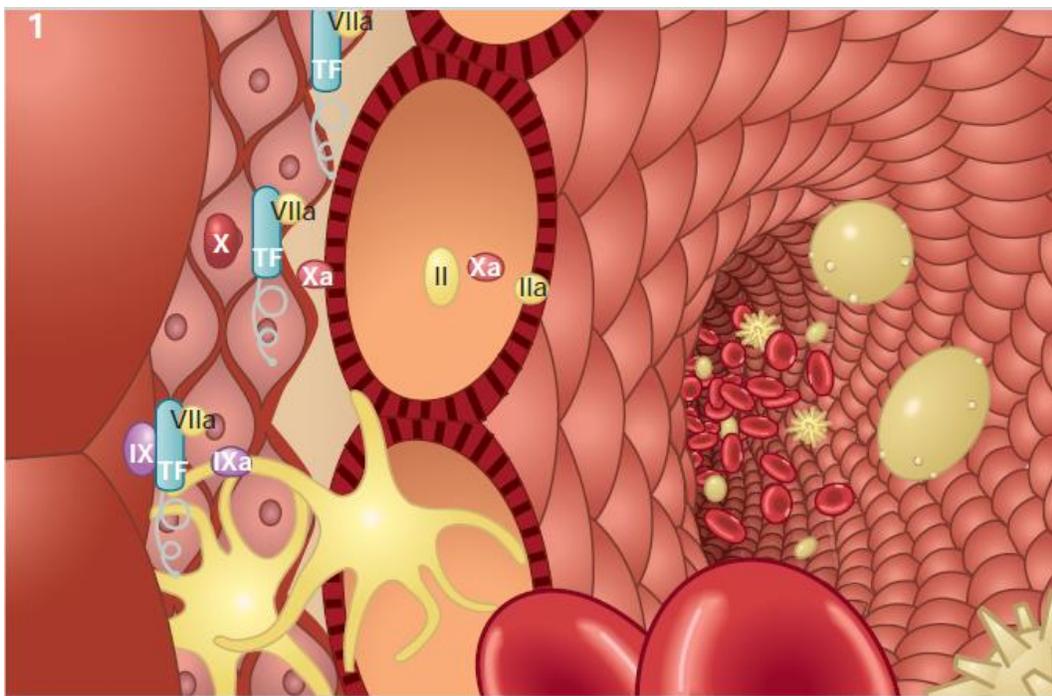


Figure 6. Current concepts of coagulation (Propagation phase).

- **Initiation:** TF in damaged vessel binds to factor VIIa, and activates factor IX and factor X. This activation of factor IX by TF-VIIa complex serves as the bridge between extrinsic and intrinsic pathways. Factor Xa then binds to factor II to form thrombin (factor IIa). Thrombin generation through this reaction is not strong and can be effectively terminated by TFPI.
- **Amplification:** Thrombin formed during initiation activates platelets, releasing FV from the  $\alpha$ -granules, and activates FXI, FVIII, and FV on the activated platelet surface.
- **Propagation:** The accumulated tenase and prothrombinase complex on platelet surface support increased amounts of thrombin generation and platelet activation.
- **Stabilization:** Thrombin generation leads to activation of factor XIII and provides strength and stability to fibrin incorporated in platelet plug. In addition, thrombin activates thrombin activatable fibrinolysis inhibitor (TAFI) that protects the clot from fibrinolysis.



**Stage 1.** Perforation results in delivery of blood and circulating factor VIIa and platelets to an extravascular space rich in membrane-bound TF. Platelets adhere to collagen and VWF associated with the extravascular tissue, and TF binds factor VIIa, thereby initiating the process of activation of factors IX and X. Factor Xa activates small amounts of prothrombin to thrombin, which in turn activates more platelets and converts factors V and VIII to factors Va and VIIIa.

**Stage 2.** The reaction is propagated by platelet-bound intrinsic factor Xase and prothrombinase, with the former being the principal generator of factor Xa. Initial clotting occurs and fibrin begins to fill in the void in cooperation with activated platelets.

**Stage 3.** A barrier composed of activated platelets laden with procoagulant complexes and enmeshed in fibrin is formed. The reaction is terminated by consumption of reagents, which attenuates further generation of thrombin, but functional procoagulant enzyme complexes persist because they are protected from the dynamic inhibitory processes of thrombomodulin.

**Stage 4.** Enzymes escaping from the plugged perforation are captured by AT-heparan complexes, and the protein C system is activated by binding of residual thrombin to endothelial cell thrombomodulin, thereby initiating the dynamic anticoagulant system. These intravascular processes work against occlusion of the vessel despite continuous resupply of reactants across the intravascular face of the thrombus.

