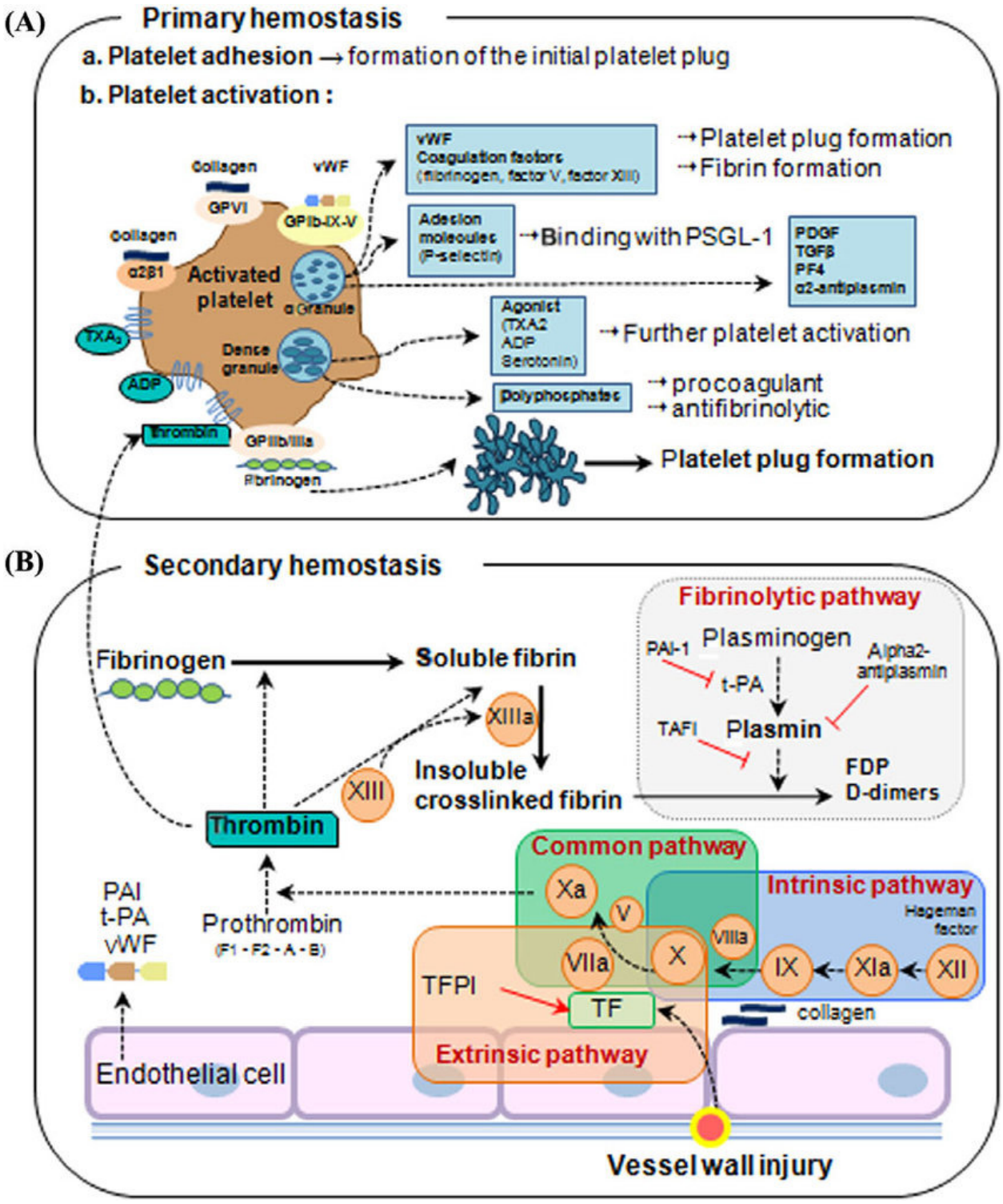
BLOOD COAGULATION UG HONS/SEM 4/SDG

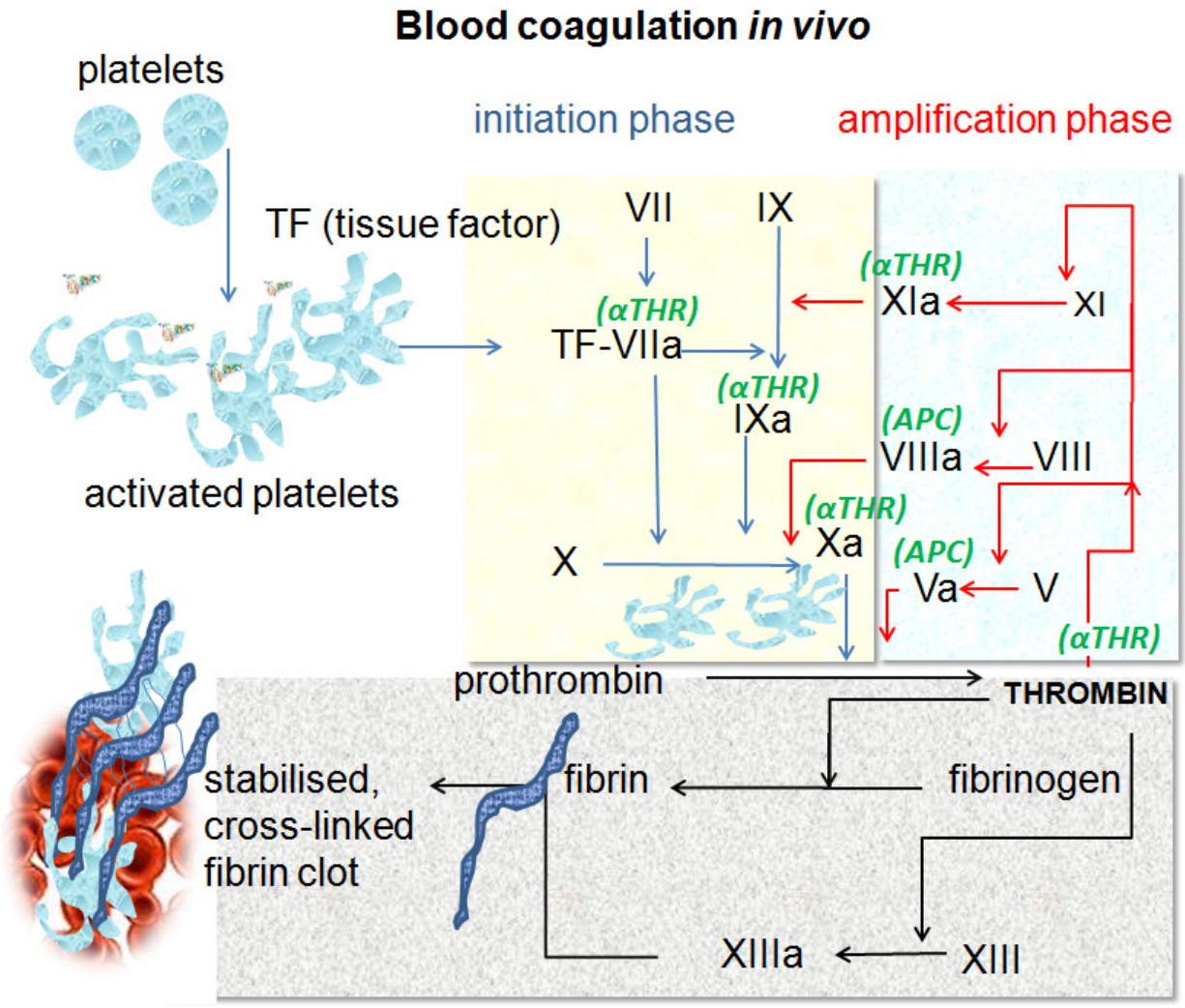
CLOTTING FACTORS

Clotting factor number	Clotting factor name	Function	Plasma half-life (h)	Plasma concentration (mg/L)
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		-

HMWK – High molecular weight kininogen; vWf – Von Willebrand factor; TF – Tissue factor



PRIMARY AND SECONDARY HEMOSTASIS



The modern time-based structuring of blood coagulation provides more authentic description of the coagulation process. It is now appreciated that the classic theories may provide only a reasonable model of in vitro coagulation tests (i.e., aPTT and PT).

Extrinsic pathway

It is considered as the first step in plasma mediated haemostasis.

It is activated by TF, which is expressed in the subendothelial tissue.

Under normal physiological conditions, normal vascular endothelium minimises contact between TF and plasma procoagulants, but vascular insult expose TF which binds with factor VIIa and calcium to promote the conversion of factor X to Xa.

Intrinsic pathway

It is a parallel pathway for thrombin activation by factor XII.

It begins with factor XII, HMW kininogen, prekallekerin and factor XI, which results in activation of factor XI.

Activated factor XI further activates factor IX, which then acts with its cofactor (factor VIII) to form tenase complex on a phospholipid surface to activate factor X.

Common pathway

Activated factor X along with its cofactor (factor V), tissue phospholipids, platelet phospholipids and calcium forms the prothrombinase complex which converts prothrombin to thrombin.

This thrombin further cleaves circulating fibrinogen to insoluble fibrin and activates factor XIII, which covalently crosslinks fibrin polymers incorporated in the platelet plug.

This creates a fibrin network which stabilises the clot and forms a definitive secondary haemostatic plug.[Figure 1]

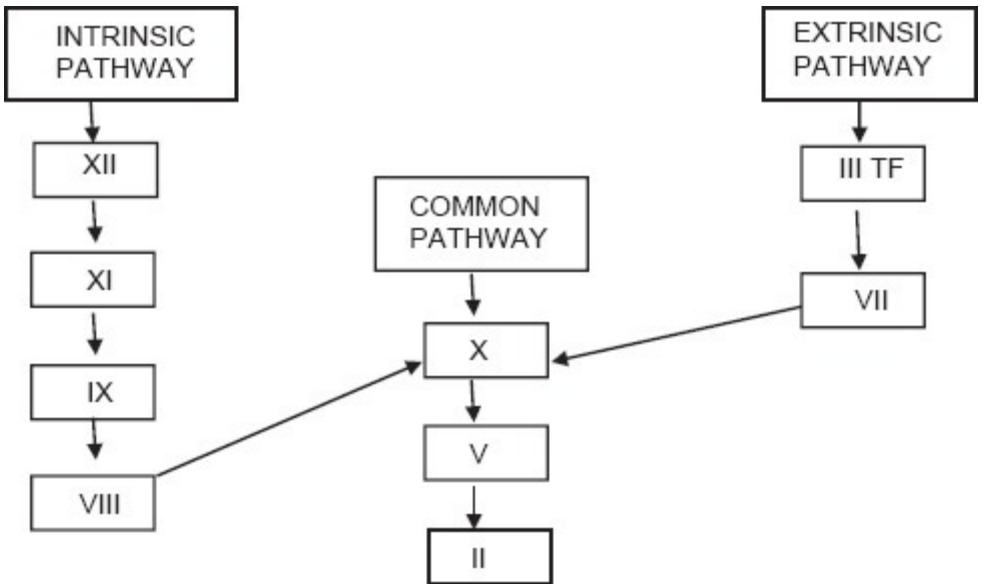


Figure 1

Earlier concept of coagulation

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.

Newer model describes coagulation with following steps:

Initiation

- It occurs by expression of TF in damaged vessel which binds factor VIIa to activate factor IX and factor X.
- This activation of factor IX by TF-VIIa complex serves as the bridge between classical extrinsic and intrinsic pathways.
- Factor Xa then binds to factor II to form thrombin (factor IIa).
- Thrombin generation through this reaction is not robust and can be effectively terminated by TF pathway inhibitor [Figure 2].

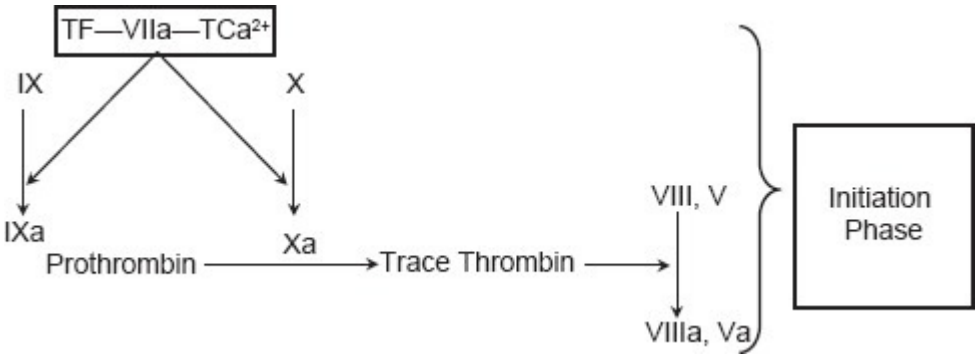


Figure 2

Current concept of coagulation (initiation phase)

Amplification

- Since the amount of thrombin generated is not sufficient, therefore numerous positive feedback loops are present that bind thrombin with platelets.
- Thrombin that is generated in the initiation phase further activates factor V and factor VIII, which serves as a cofactor in prothrombinase complex and accelerates the activation of Factor II by F Xa and of F Xa by F IXa, respectively.

Propagation

- The accumulated enzyme complexes (tenase complex and prothrombinase complex) on platelet surface support robust amounts of thrombin generation and platelet activation.
- This ensures continuous generation of thrombin and subsequently fibrin to form a sufficiently large clot [Figure 3].

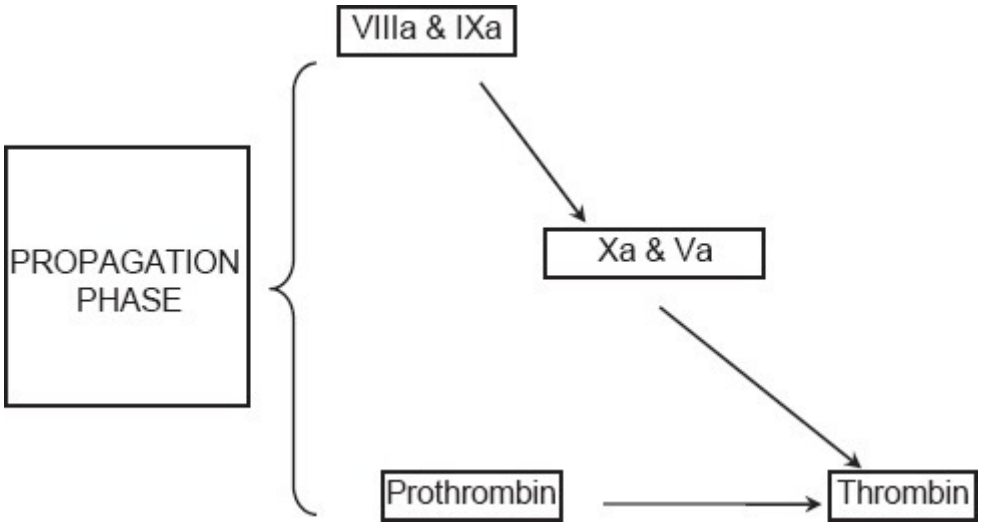


Figure 3

Current concepts of coagulation (propagation phase)

Stabilization

- Thrombin generation leads to activation of factor XIII (fibrin stabilizing factor) which covalently links fibrin polymers 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.