Hemostasis

When a small blood vessel is transected or injured a spontaneous and natural process occur to arrest bleeding process is called **hemostasis** . It involves a series of event which leads to clot formation and prevention of further blood loss these include

contraction of the injured vessel

formation of platelets plug at the site of injury

Activation of blood coagulation

Activation of fibrinolytic system which gradually dissolves away the fibrin clot as tissue repair is taking place
Repair of the vessel wall occurs by the proliferation of smooth muscle cells and fibroblasts , the deposition of new connective tissue matrix and growth of new luminal lining of endothelial cells .

1- contraction of the vessel wall (vasoconstriction): this reduces the flow of blood from the vessel rupture. Most of vasoconstriction result probably from direct of injury upon vascular smooth muscle cells. vasoconstrictor substance released from the platelets also contribute to this vasoconstriction.

2- Formation of platelets plug: when platelets come in contact with the exposed collagen of the blood vessel, they become activated , they begin to swell , put out pseudopodia , become sticky and adhere to collagen and release different substances such serotonin, and ADP.

Their enzyme form thromboxane A2. serotonin and thromboxane A2 enhance vasoconstriction. ADP and thromboxane A2 activate other nearby platelets and this causes circulating platelets to adheres to the platelets already attached to the collagen ,so platelets will aggregate (platelets stick to each other) and form platelets plug at the site of injury.

3-Blood coagulation : platelet plug is converted into the definitive clot by formation of fibrin . The clotting mechanism responsible for the formation of fibrin involves a cascade of reactions in which inactive enzymes are activated , and the activated enzymes in turn activate other inactive enzymes .

- The clotting involved several substances known as clotting factors synthesized by liver cells or released from platelets or damaged tissues.

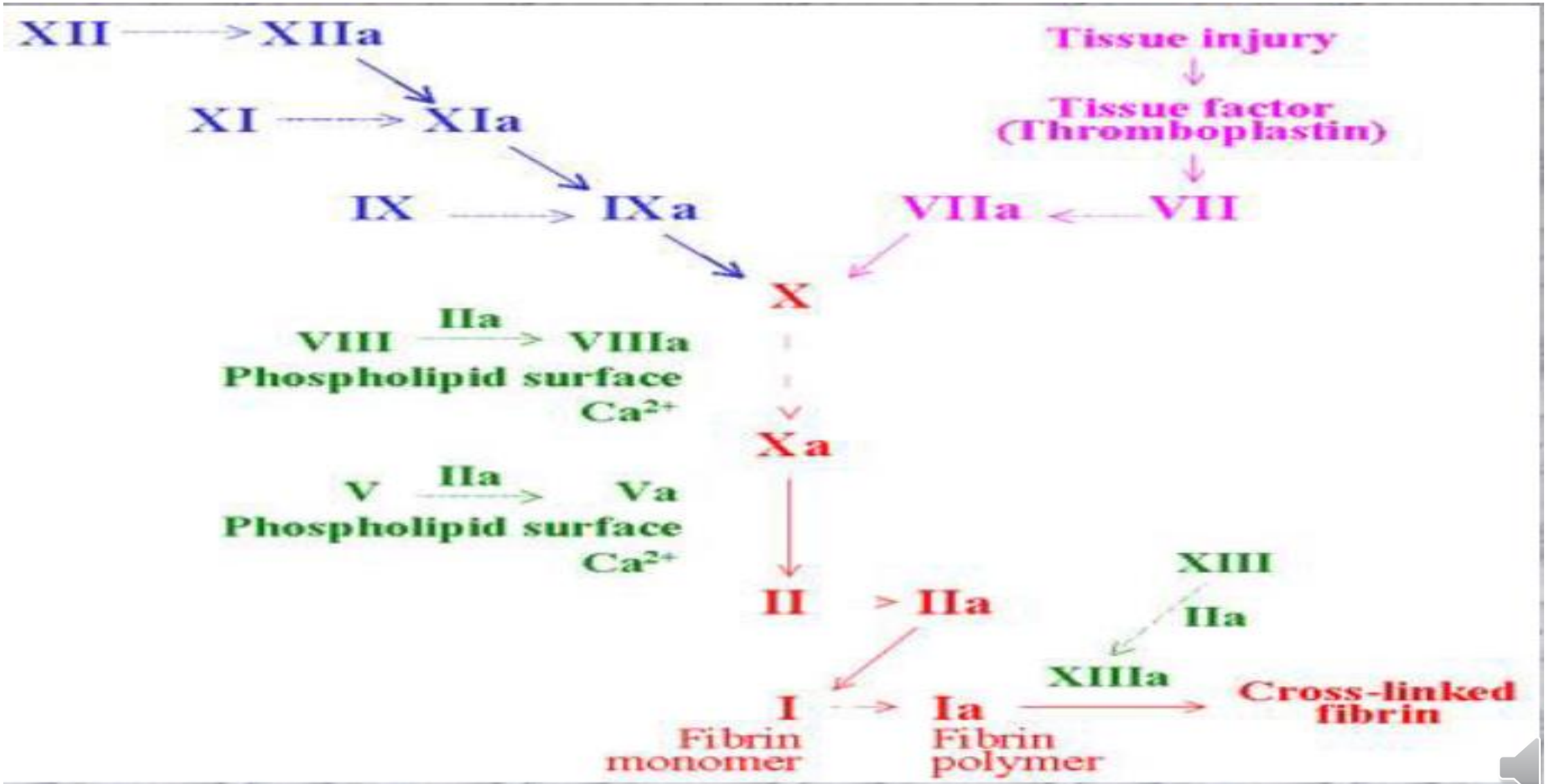
- There are three stages in clotting:

- Formation of prothrombin activator (or prothrombinase)
- Conversion of prothrombin to thrombin
- Conversion of fibrinogen to fibrin

- **Formation of prothrombin activator**: It formed by two ways:
- *1. Extrinsic pathway, which is initiated by tissue thromboplastin*
- *2. Intrinsic pathway of coagulation, initiated by platelets*
- **Extrinsic pathway**; this process occurs only *in vivo* (within the body) and is rapid process. After injury, the damaged tissue release tissue thromboplastin. It react with active factor VII (VII) in the presence of Ca ion and tissue phospholipid to form a complex. This complex convert inactive factor X to active factor X (Xa).

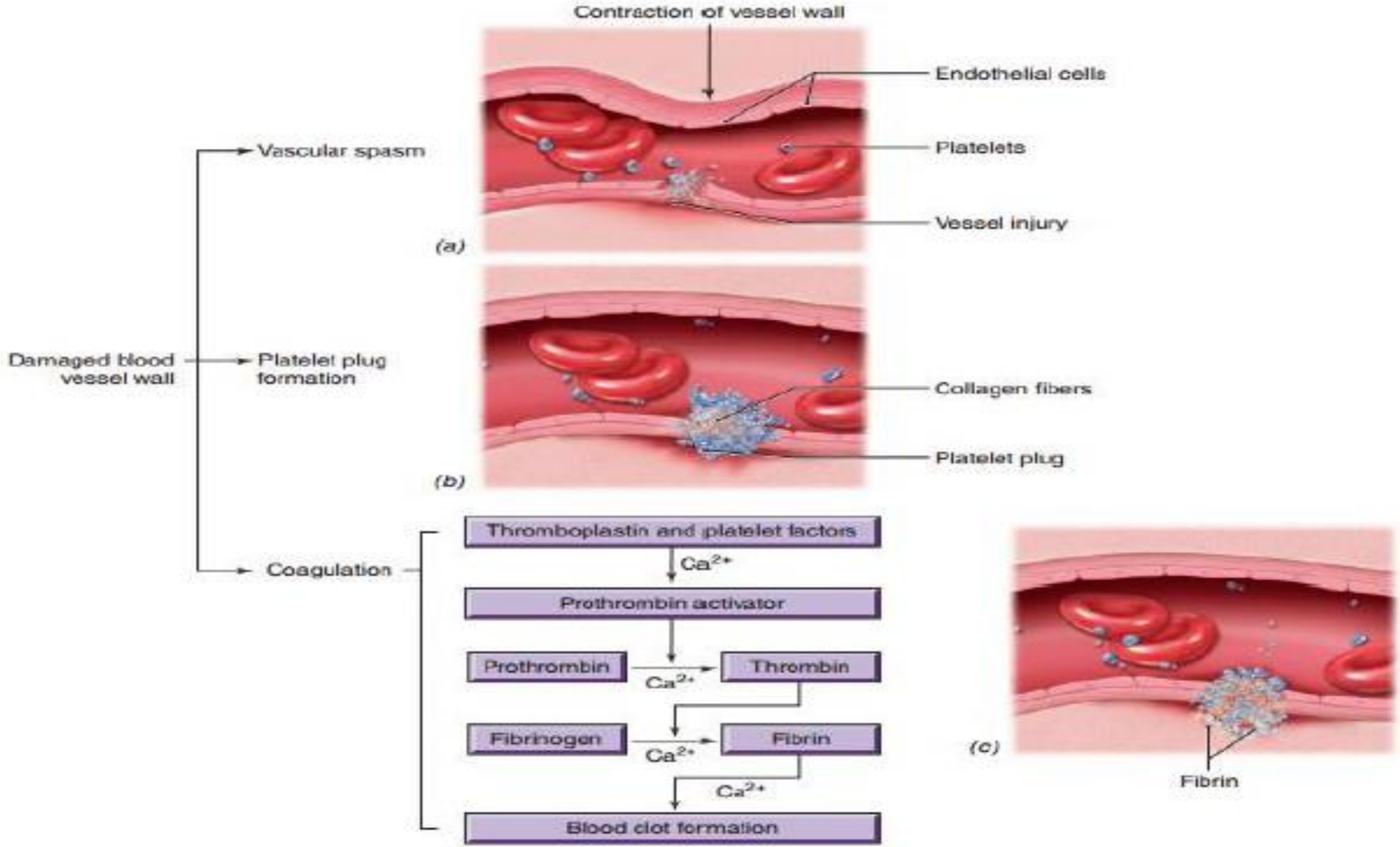
- **Intrinsic pathway**: This occur in both in vivo and in vitro. It is a slower process. When there is injury, inactive factor XII comes in contact with collagen and damaged platelets and it is activated to active factor XII (XIIa) in the presence of kallikrein (Ka). XIIa activates factor XI, which in turn activates factor IX in the presence of Ca ions. IXa form a complex. This complex with VIIIa, PF-3 (Plateletfactor-3) and Ca to form a complex. This complex convert X to Xa,

- Intrinsic and extrinsic pathways converge on a third common pathway. Xa forms a complex with Va, Ca ion and PF3 to form prothrombin activator. Inactive factor V is converted to active factor V (Va) by thrombin.


XII
XIIa
XI
XIa
IX
IXa
Tissue injury
Tissue factor
(Thromboplastin)
VIIa
VII
X
IIa
VIII
VIIIa
Phospholipid surface
Ca2+
Xa
IIa
V
Va
Phospholipid surface
Ca2+
XIII
II
IIa
IIa
XIIIa
I
Fibrin
monomer
Ia
Fibrin
polymer
Cross-linked
fibrin

Number and/or name
I (fibrinogen)
II (prothrombin)
III (tissue factor or tissue thromboplastin)
IV (calcium)
V (proaccelerin, labile factor)
VI
VII (stable factor, proconvertin)
VIII (Antihemophilic factor A)
IX (Antihemophilic factor B or Christmas factor)
X (Stuart-Prower factor)
XI (plasma thromboplastin antecedent)
XII (Hageman factor)
XIII (fibrin-stabilizing factor)

- **Formation of thrombin**
- Prothrombin activator (Prothrombinase), in the presence of Ca ion, converts prothrombin to thrombin
- **Formation of insoluble fibrin**
- Thrombin in presence of Ca ions converts soluble fibrinogen to insoluble fibrin. Thrombin also activates factor XIII which strengthens and stabilizes the fibrin threads. The fibrin threads form a network in which blood cells are entangled or trapped.


Contraction of vessel wall
Endothelial cells
Platelets
Vessel injury
(a)
Vascular spasm
Damaged blood vessel wall
Platelet plug formation
Collagen fibers
Platelet plug
(b)
Coagulation
Thromboplastin and platelet factors
Ca^{2+}
Prothrombin activator
Prothrombin
Ca^{2+}
Thrombin
Fibrinogen
Ca^{2+}
Fibrin
Ca^{2+}
Blood clot formation
(c)
Fibrin

Clot retraction :within few minutes after a clot is formed ,it beings to contract and usually expressed most of the fluid from the clot within 20-60 minutes .the fluid expressed is called **serum .** Serum differs from plasma in that it cannot clot because all its fibrinogen and most other clotting factors have been removed , and also serum has higher serotonin content because of breakdown of platelets during clotting .platelets are necessary for clot retraction to occur.

When the number of platelets in the circulating blood is low , there will be failure of blood .