Blood Coagulation

Blood coagulation or clotting is an important phenomenon to prevent excess loss of blood in case of injury or trauma. The blood stops flowing from a wound in case of injury. The blood clot or 'coagulum' is formed by a network of fibrin threads. In this network, deformed and dead formed elements (erythrocytes, leukocytes and platelets) get trapped.

Prothrombin is the inactive form of thrombin that is present in the plasma. Thrombokinase converts prothrombin to active thrombin which in turn activates fibrinogen to fibrin. All these clotting factors help in blood coagulation.

An injury stimulates platelets or thrombocytes to release various factors that initiate the blood clotting cascade. Calcium ions play an important role in blood coagulation.

Factors Involved in Blood Coagulation

Coagulation of blood occurs through a series of reactions due to the activation of a group of substances called clotting factors. There are 13 clotting factors identified and named after the scientists who discovered them or as per the activity. Only factor IX or Christmas factor is named after the patient in whom it was discovered.

Factor I Fibrinogen	Factor VI Unassigned	Factor XI Plasma thromboplastin antecedent
Factor II Prothrombin	Factor VII Stable factor	Factor XII Hageman factor
Factor III Thromboplastin	Factor VIII Antihemophilic factor	Factor XIII Fibrin–stabilising factor
Factor IV Calcium Factor	Factor IX Christmas factor	
Factor V Labile factor (Proaccelerin)	Factor X Stuart–Prower factor	

Blood Coagulation Pathway

The process of blood coagulation leads to haemostasis, i.e. prevention of bleeding or haemorrhage. Blood clotting involves activation and aggregation of platelets at the exposed endothelial cells, followed by deposition and stabilisation of cross-linked fibrin mesh.

Primary haemostasis involves platelet aggregation and formation of a plug at the site of injury, and secondary haemostasis involves strengthening and stabilisation of platelet plug by the formation of a network of fibrin threads. The secondary haemostasis involves two coagulation pathways, the intrinsic pathway and the extrinsic pathway. Both pathways merge at a point and lead to the activation of fibrin, and the formation of the fibrin network.

Platelet Activation

The blood circulating in the blood vessel does not clot under normal circumstances. The blood coagulation process is stimulated when there is any damage to the endothelium of blood vessels. It leads to platelet activation and aggregation. When collagen is exposed to the platelets due to injury, the platelets bind to collagen by surface receptors. This adhesion is stimulated by the von Willebrand factor released from endothelial cells and platelets. This forms additional cross-linking and activation of platelet integrins, which facilitate tight binding and aggregation of platelets at the site of injury. This leads to primary haemostasis.

Blood Coagulation Cascade

The process of coagulation is a cascade of enzyme catalysed reactions wherein the activation of one factor leads to the activation of another factor and so on.

The three main steps of the blood coagulation cascade are as follows:

Formation of prothrombin activator

Conversion of prothrombin to thrombin

Conversion of fibrinogen into fibrin

1. **Formation of prothrombin activator**

The formation of a prothrombin activator is the first step in the blood coagulation cascade of secondary haemostasis. It is done by two pathways, viz. extrinsic pathway and intrinsic pathway.

Extrinsic Coagulation Pathway

It is also known as the tissue factor pathway. It is a shorter pathway. The tissue factors or tissue thromboplastins are released from the damaged vascular wall. The tissue factor activates the factor VII to VIIa. Then the factor VIIa activates the factor X to Xa in the presence of Ca2+.

Intrinsic Coagulation Pathway

It is the longer pathway of secondary haemostasis. The intrinsic pathway begins with the exposure of blood to the collagen from the underlying damaged endothelium. This activates the plasma factor XII to XIIa.

XIIa is a serine protease, it activates the factor XI to Xia. The Xia then activates the factor IX to IXa in the presence of Ca2+ ions.

The factor IXa in the presence of factor VIIIa, Ca2+ and phospholipids activate the factor X to Xa.

Common Pathway

The factor Xa, factor V, phospholipids and calcium ions form the prothrombin activator. This is the start of the common pathway of both extrinsic and intrinsic pathways leading to coagulation.

2. **Conversion of prothrombin to thrombin**

Prothrombin or factor II is a plasma protein and is the inactive form of the enzyme thrombin. Vitamin K is required for the synthesis of prothrombin in the liver. The prothrombin activator formed above converts prothrombin to thrombin. Thrombin is a proteolytic enzyme. It also stimulates its own formation, i.e. the conversion of prothrombin to thrombin. It promotes the formation of a prothrombin activator by activating factors VIII, V and XIII.

3. Conversion of fibrinogen into fibrin

Fibrinogen or factor I is converted to fibrin by thrombin. Thrombin forms fibrin monomers that polymerise to form long fibrin threads. These are stabilised by the factor XIII or fibrin stabilising factor. The fibrin stabilising factor is activated by thrombin to form factor XIIIa. The activated fibrin stabilising factor (XIIIa) forms cross-linking between fibrin threads in the presence of Ca2+ and stabilises the fibrin meshwork. The fibrin mesh traps the formed elements to form a solid mass called a clot.