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Hemostasis and Blood Coagulation

The term hemostasis means prevention of blood loss. This achieved by several mechanisms, including:

1. **Vascular spasm.**
2. **Formation of a platelets plug.**
3. **Formation of blood clot.**
4. **Growth of fibrous tissue into the blood clot to close the whole vessel permanently.**

Vascular Spasm

The most immediate protection against blood loss is vascular spasm, a prompt constriction of the broken vessel. Several things trigger this reaction. An injury stimulates with pain receptors, some of which directly innervate nearby blood vessels and cause them to constrict. Immediately after a blood vessel is cut or ruptured, the stimulus of the trauma to the vessel causes the wall of the vessel to contract due to nervous reflexes, local myogenic spasm and local humoral factors from blood platelets.

Formation of a Platelet Plug.

Platelets are not cells, but small fragments of megakaryote cytoplasm. Although they were once called thrombocytes. Platelets are small round or oval discs 2-4 µm in diameter.

They are formed in the bone marrow from megakaryocytes which are extremely large cells of the hemopoietic series in the bone marrow that fragment into platelets. The normal concentration of platelets in the blood is between 150,000 and 400,000 per µL.

Platelets have many functional, even through these do not have nuclei and can not reproduce. In their cytoplasm are such active factor as:

1. **They secrete growth factors that stimulate mitosis in fibroblasts and smooth muscle and help to maintain the linings of blood vessels.**

2. **They secrete vasoconstrictors that cause vascular spasm in broken vessels.**

3. **They form temporary platelet plugs to stop bleeding.**

4. **They phagocytize and destroy bacteria.**

5. **They secrete chemicals that attract neutrophils and monocytes to sites of inflammation.**

6. **They dissolve blood clots that have outlasted their usefulness.**

The cell membrane of the platelets is also important, on its surface is a coat of glycoproteins that causes it to avoid adherence to normal endothelium and yet to adhere to injured areas of the vessel wall.

Mechanism of the Platelet Plug

Platelet repair of vascular openings is based on several important functions of the platelet itself, when platelets come in contact with a damaged vascular surface, such as the collagen fibers in the vascular wall or damaged endothelial cells, they immediately change their characteristics. They begin to swell, they assume irregular forms and become sticky so that they stick to the collagen fibers, they secrete large quantities of ADP and their enzymes form thromboxane A2 in turn act on nearby platelets to activate them as well forming a platelet plug.

Formation of Blood Clot

The clot begins to develop in 15 seconds, if trauma of the vascular wall has been severe, and in 1-2 minutes if it is minor.

Mechanism of Blood Coagulation

The clotting takes place in three steps:

1. **In response to rupture of the vessel or damage to the blood, the complex of activated substances collectively called prothrombin activator.**
2. **The prothrombin activator catalyzes the conversion of prothrombin into thrombin.**
3. **The thrombin acts an enzyme to convert fibrinogen into fibrin fibers, that enmesh platelets, blood cells and plasma to form the clot.**

Conversion of Prothrombin to Thrombin :

Prothrombin is a plasma protein, an alpha 2- globulin, having a molecular weight of 68,700. it is present in normal plasma in a concentration 15 mg/dl. It is unstable protein that can easily split into thrombin which has a molecular weight 33,700 in presences of prothrombin activator and calcium ions.

Prothrombin is formed by the liver, vitamin K is required by the liver for normal formation of prothrombin.

Conversion of Fibrinogen to Fibrin

Fibrinogen is a high-molecular weight protein (340,000) that occurs in the plasma in quantities of 100-700 mg/dl. It's formed in the liver.
Thrombin is a protein enzyme with proteolytic capabilities, it act on fibrinogen to remove four low-molecular weight peptides from each

molecule of fibrinogen, forming a molecule of fibrin monomer that has the automatic capability of polymerizing with other fibrin molecule forming long fibrin fibers that form the reticulum of clot. There are two reaction pathways to coagulation, one of them, extrinsic mechanism, is initiated by clotting factors released by the damaged blood vessel and perivascular tissues. The reaction pathway it use only clotting factors found in the blood itself called intrinsic mechanim.

The extrinsic mechanism is the damage of blood vessel release lipoprotein mixture called thromboplastin (factor III) in the presences of Ca , thromboplatin activates factor VII, which then activates factor X. the extrinsic and intrinsic pathways differ only in how they arrive at active factor X.

The intrinsic mechanism, when platelets degranulate, they release factor XII (Hageman factor) and then this leads to activated factors XI, IX and VIII, in that order, each serving as an enzyme that catalyzes the next step and finally to factor X. This pathway also requires calcium ions and platelet thomboplastic factor (PF3).

Once factor X is activated, the remaining events are identical in the intrinsic and extrinsic mechanisms. Factor X combines with factors III and V in the presence of (Ca and PF3) to produce an enzyme, prothombin activator, this enzyme acts on a globulin called prothrombin (factor II) , converting it to enzyme thrombin. Thrombin then converts fibrinogen to fibrin. Fibrin forms a loose mesh at first, but factor VIII causes the formation of covalent cross-links that convert this to fibrin polymer – a dense aggregation of fibers that forms the structural basis of the clot.

The especially important difference between extrinsic and intrinsic pathway is the extrinsic can explosive nature, once initiated, its speed of occurrence is limited only by the amount of tissue factor released from the traumatized tissues and by the quantities of factor X, VII and V in the blood. With severe trauma, clotting can occur in 15 seconds. While intrinsic usually 1-6 minutes to cause clotting.

Clot Formation