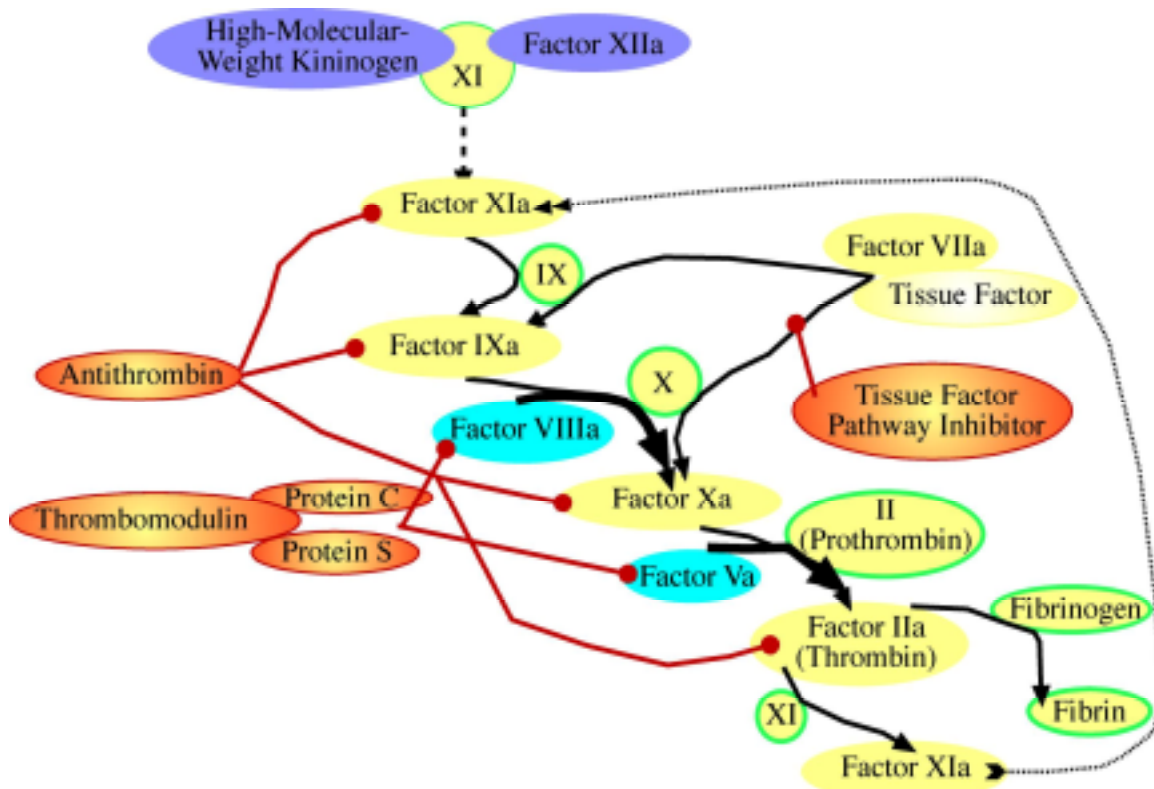


The Clotting Process (Hemostasis)

The process by which the body prevents blood loss is referred to as coagulation. Coagulation involves the formation of a blood clot (thrombus) that prevents further blood loss from damaged tissues, blood vessels or organs. This is a complicated process with a cellular system comprised of cells called platelets that circulate in the blood and serve to form a platelet plug over damaged vessels and a second system based upon the actions of multiple proteins (called clotting factors) that act in concert to produce a fibrin clot. These two systems work in concert to form a clot; disorders in either system can yield disorders that cause either too much or too little clotting.

Platelets serve three primary functions: 1) sticking to the injured blood vessel (called platelet adherence), 2) attaching to other platelets to enlarge the forming plug (called platelet aggregation), and 3) providing support (molecules on the surface of platelets are required for many of the reactions) for the processes of the coagulation cascade.

When a break in a blood vessel occurs, substances are exposed that normally are not in direct contact with the blood flow. These substances (primarily collagen and von Willebrand factor) allow the platelets to adhere to the broken surface. Once a platelet adheres to the surface, it releases chemicals that attract additional platelets to the damaged area, referred to as platelet aggregation. These two processes are the first responses to stop bleeding. The protein based system (the coagulation cascade) serves to stabilize the clot that has formed and further seal up the wound.



The diagram on the previous page shows many of the reactions in the coagulation cascade that are necessary to form a clot. As noted above, the third role of the platelet is to support the coagulation cascade. This support is provided, in part, by one of the components of the outside of a platelet, called phospholipids (lipid=fat), which are required for many of the reactions in the clotting cascade.

The goal of the cascade is to form fibrin, which will form a mesh within the platelet aggregate to stabilize the clot. All of the factors have an inactive and an active form. Once activated, the factor will serve to activate the next factor in the sequence until fibrin is formed.

The coagulation cascade takes place at the site of a break in a blood vessel that has the platelet aggregate. Tissue factor and factor VIIa (the 'a' denotes the active form of the factor) activate factor X, forming factor Xa. Factor Xa is then able to activate prothrombin (also referred to as factor II) to form thrombin (factor IIa). Thrombin converts fibrinogen to fibrin (factors I and Ia respectively). Fibrin forms a mesh that, in concert with the platelets, plugs the break in the vessel wall. The fibrin mesh is further stabilized by factor XIII, which sews up the clot (much like forming an intricate network of cross-stitched strands of fibrin).

There are multiple other interactions detailed on the above diagram. All of these interactions (and others) are required for coagulation to work properly. For the purposes of understanding clotting disorders, there are several that need to be discussed.

Factors that Accelerate Clot Formation:

Factor V and factor VIII (shown in light green) accelerate the conversion of factor X to factor Xa by factor IXa (this is done by factor VIII) and accelerate the conversion of prothrombin to thrombin as done by factor Xa.

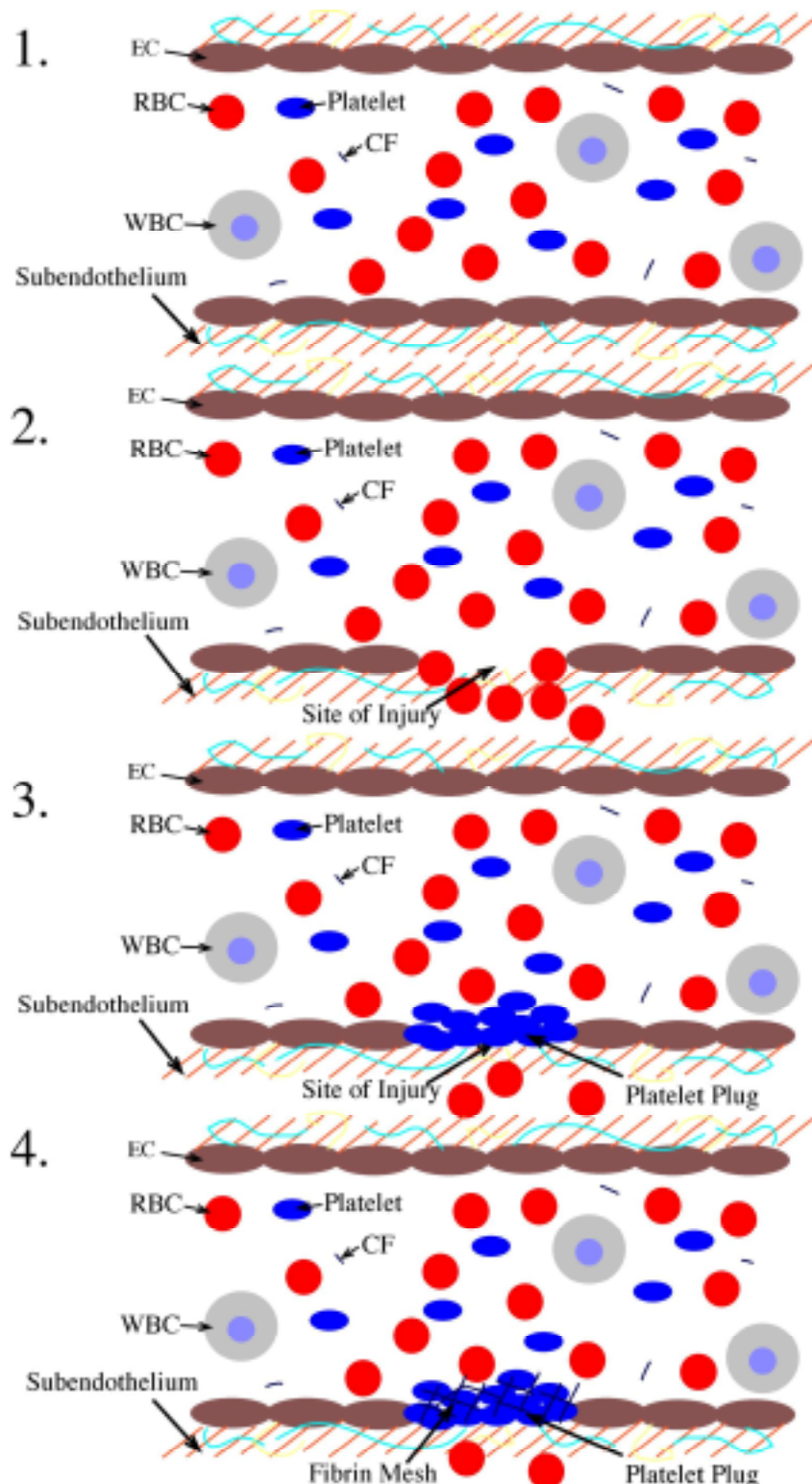
Factors that Inhibit (Slow Down) Clot Formation:

Protein C, protein S and thrombomodulin form a complex (group of proteins) that can inactivate factor VIII and factor V. The protein C, protein S and thrombomodulin complex is activated by thrombin.

Antithrombin (formerly called antithrombin III) serves to block the actions of multiple clotting factors (called inhibition). Inhibition is depicted with the red lines that end in a filled circle. The filled circle denotes the factor that is inhibited.

Tissue factor pathway inhibitor works to inhibit the formation of factor Xa.

All of the above interactions are required in order to maintain the hemostatic balance (hemo=blood, stasis=state of not flowing/moving), which prevents excessive bleeding or excessive clotting. The following page depicts the overall process by which hemostasis (clotting) occurs at the site of injury to a blood vessel.



The Formation of a Clot. Panel 1 depicts a normal artery or vein in the body composed of an endothelial cell (EC) wall with a subendothelial layer of collagen and other substances. Some of the normal components of the blood are depicted including red blood cells (RBC), white blood cells (WBC), platelets and clotting factors (CF). Panel 2 shows a break in the EC wall, resulting in bleeding from the site. Panel 3 shows platelets coming together (aggregation) to form a platelet plug. Panel 4 shows the final step, where the coagulation cascade forms a fibrin network to secure the clot in place.

Further Information:

For further information, please visit the University of Illinois – Urbana/Champaign and Carle Cancer Center webpages on coagulation disorders at:

www-admin.med.uiuc.edu/hematology.

This information is provided as a resource to patients and health care providers. The information contained above represents common diagnostic and treatment modalities, but individual circumstances may require additional or different tests or medications. All medical decisions should be made with the advice and consultation of a physician or other health care provider.