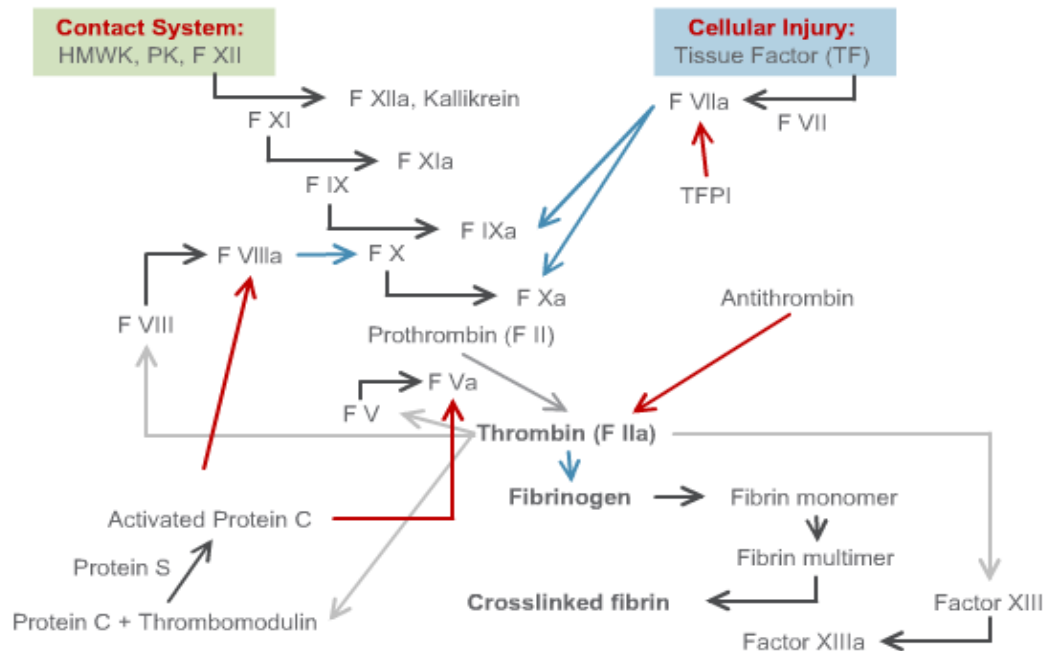


# Steps in the Coagulation Pathway



Normal hemostasis requires a delicate balance between the procoagulant and anticoagulant systems. The function of the procoagulant system is to form a hemostatic plug, out of platelets and fibrin, within the inside lining of the injured blood vessel. The function of the anticoagulant system is to confine the hemostatic plug to the injured site. The anticoagulant system also prevents the formation of a pathologic thrombus that occludes the lumen of the vessel or that embolizes and occludes distant vessels.<sup>1</sup>

The procoagulant system is triggered when a vessel wall is injured and tissue factor is exposed to circulating blood. Tissue factor binds with activated factor VII to form a complex. This complex activates factors IX and X. Factor IXa binds factor VIIIa to form a second complex which also activates factor X. Factor Xa binds factor Va to form the prothrombinase complex. This complex converts prothrombin to thrombin. Thrombin cleaves fibrinogen to form insoluble fibrin strands in the final steps in the coagulation pathway. It also activates platelets and amplifies coagulation by proteolytically activating factors V and VIII. Together factors Va and VIIIa can potentially increase the rate of thrombin generation by one million-fold. They also provide major control points in the regulation of thrombin generation.<sup>2,3</sup>

The anticoagulant system is activated in parallel with the procoagulant system. Protein C is activated by the thrombin-thrombomodulin complex. Activated protein C inactivates factors Va and VIIIa in the presence of protein S. Antithrombin irreversibly inhibits thrombin by covalently binding to the thrombin enzymatic active site.<sup>2,3</sup>

Both of these systems, the procoagulant and anticoagulant system, can be disrupted by acquired disorders, environmental factors, and variations in genes.<sup>3</sup>

1. Information Source: <http://www.hematology.org/publications/hematologist/SO06/cover.cfm>
2. Mehta AB, Hoffbrand AV. (2000) Haematology at a glance. Oxford; Malden, Mass.: Blackwell Science.
3. Turpie AG, Chin BA, Lip GY. (2002) ABC of antithrombotic therapy: Venous thromboembolism: pathophysiology, clinical features, and prevention. BMJ 325:887-890.