

reactions in which the enzymatically active product subsequently converts the downstream inactive protein into an active serine protease. In addition, the activation of thrombin leads to stimulation of platelets. HK, high-molecular-weight kininogen; PK, prekallikrein; TF, tissue factor.

The coagulation cascade is primarily initiated by vascular injury exposing tissue factor to blood components ([Fig. 117-2](#)). Tissue factor may also be found in bloodborne cell-derived microparticles and, under pathophysiologic conditions, in leukocytes or platelets. Plasma factor VII (FVII) is the ligand for and is activated (FVIIa) by binding to tissue factor exposed at the site of vessel damage. The binding of FVII/FVIIa to tissue factor activates the downstream conversion of factor X (FX) to active FX (FXa). In an alternative reaction, the FVII/FVIIa–tissue factor complex initially converts FIX to FIXa, which then activates FX in conjunction with its cofactor factor VIII (FVIIIa). Factor Xa with its cofactor FVa converts prothrombin to thrombin, which then converts soluble plasma fibrinogen to insoluble fibrin, leading to clot or thrombus formation. Thrombin also activates FXIII to FXIIIa, a transglutaminase that covalently cross-links and stabilizes the fibrin clot. Formation of thrombi is affected by mechanisms governing fibrin structure and stability, including specific fibrinogen variants and how they alter fibrin formation, strength, and structure.

Several antithrombotic factors also regulate coagulation; these include antithrombin, tissue factor pathway inhibitor (TFPI), heparin cofactor II, and protein C/protein S. Under normal conditions, these factors limit the production of thrombin to prevent the perpetuation of coagulation and thrombus formation. Typically, after the clot has caused occlusion at the damaged site and begins to expand toward adjacent uninjured vessel segments, the anticoagulant reactions governed by the normal endothelium become pivotal in limiting the extent of this hemostatically protective clot.

■ RISK FACTORS FOR VENOUS THROMBOSIS

An array of different factors contributes to the risk of VTE, and it is notable that women and men of all ages, races, and ethnicities are at risk for VTE. The risk factors for venous thrombosis are primarily related to hypercoagulability, which can be genetic ([Table 117-1](#)) or